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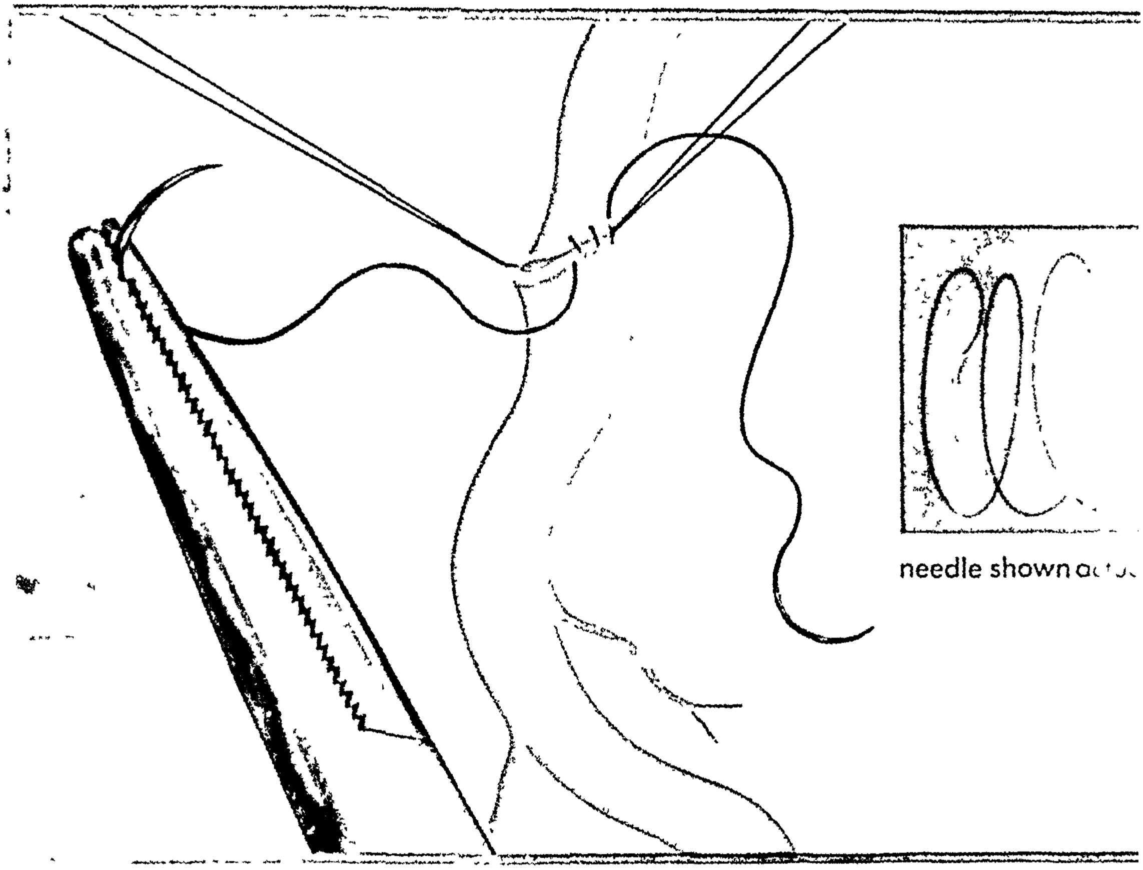

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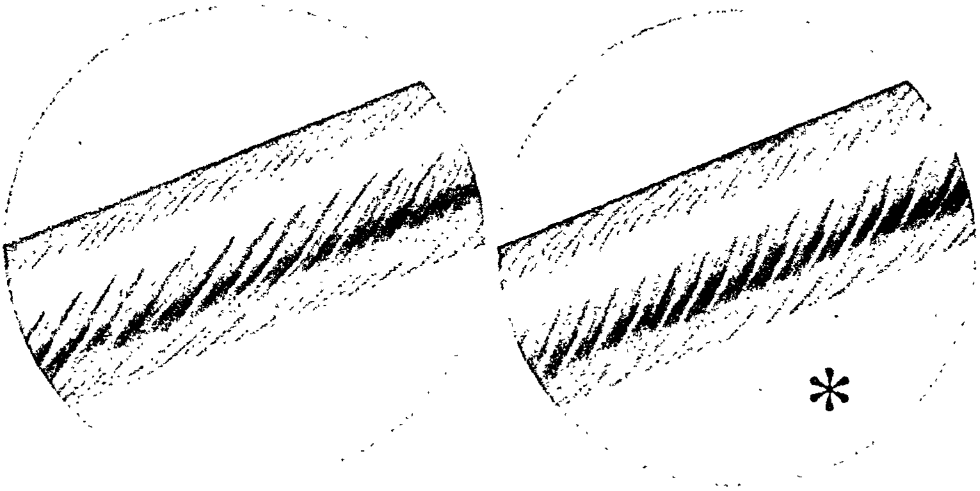

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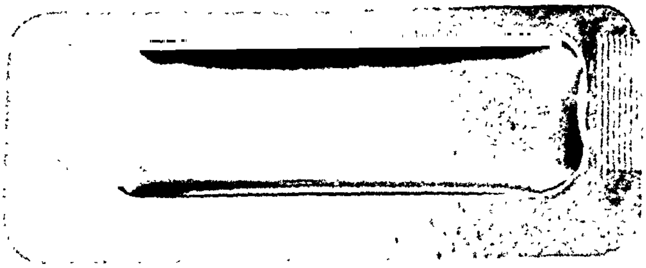

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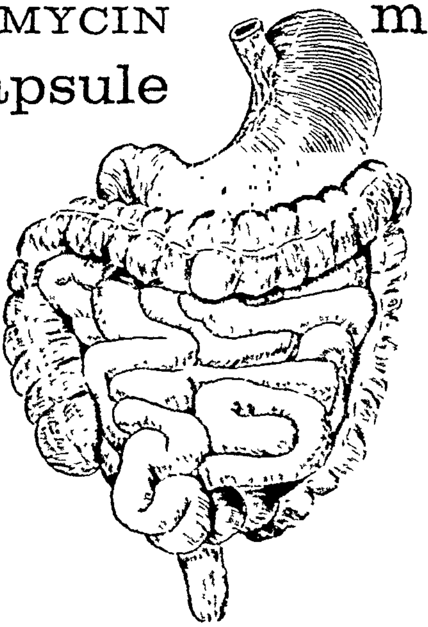

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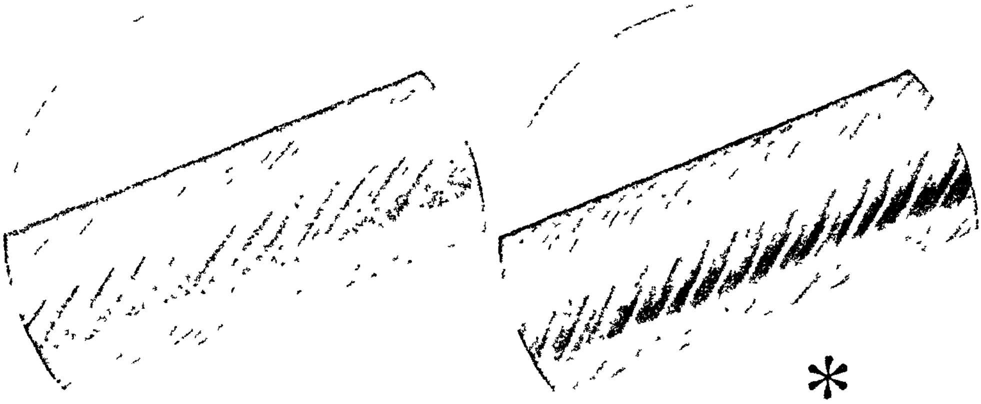

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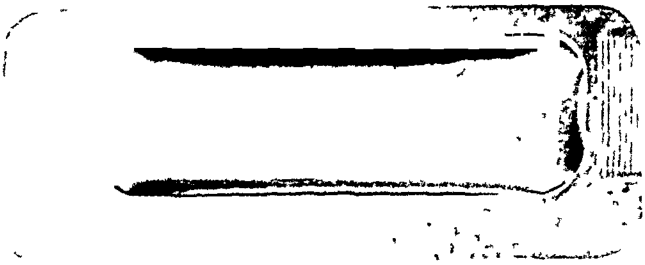

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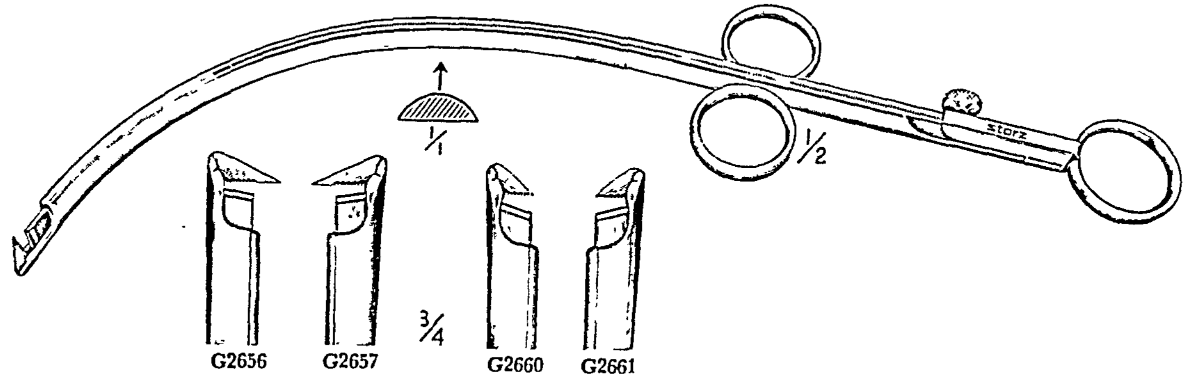

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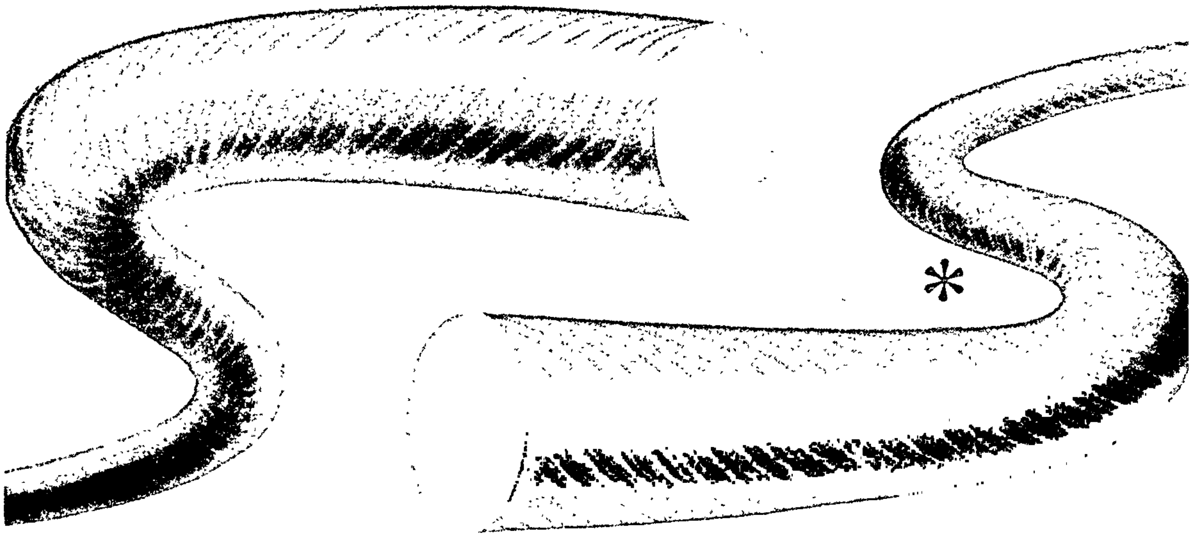

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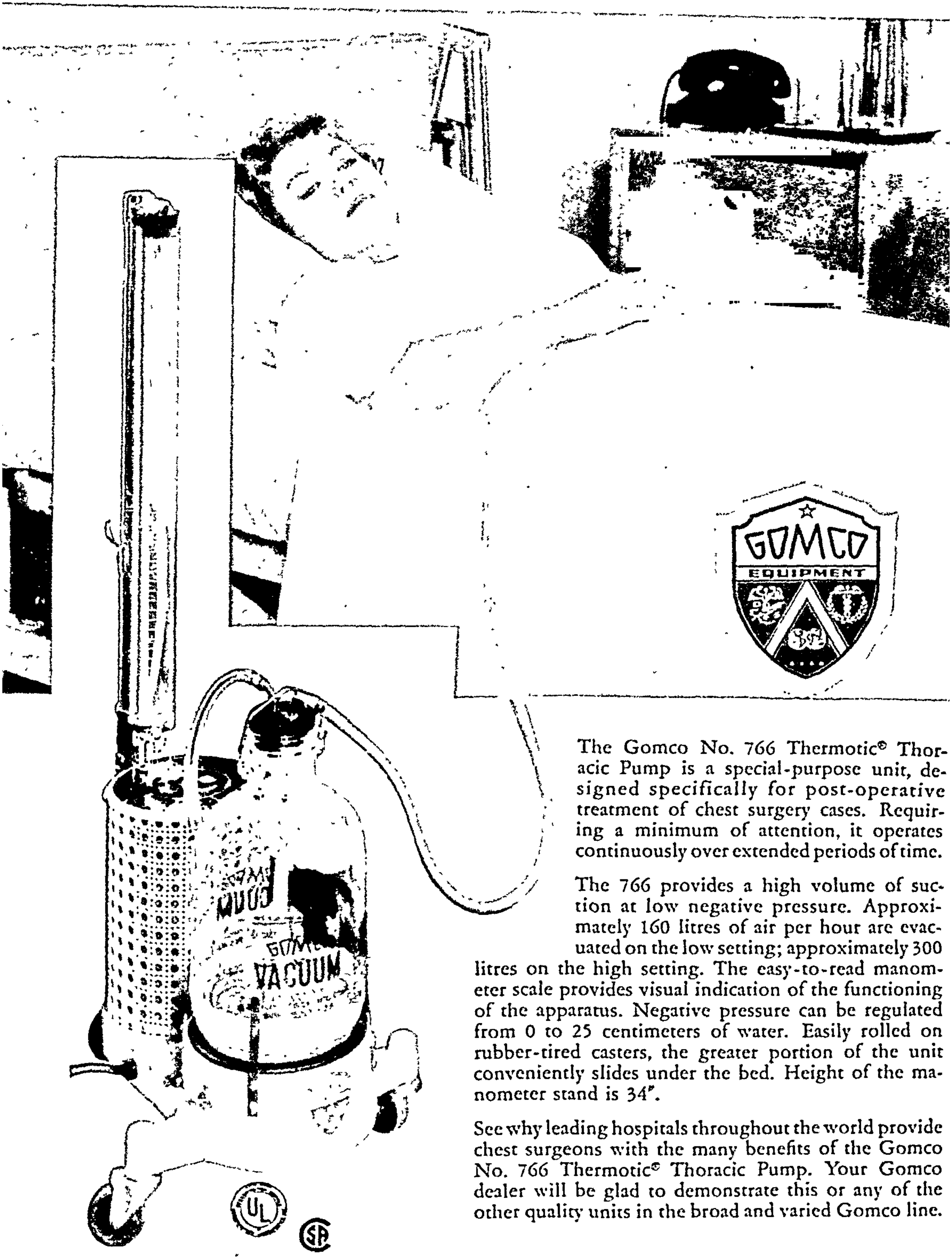

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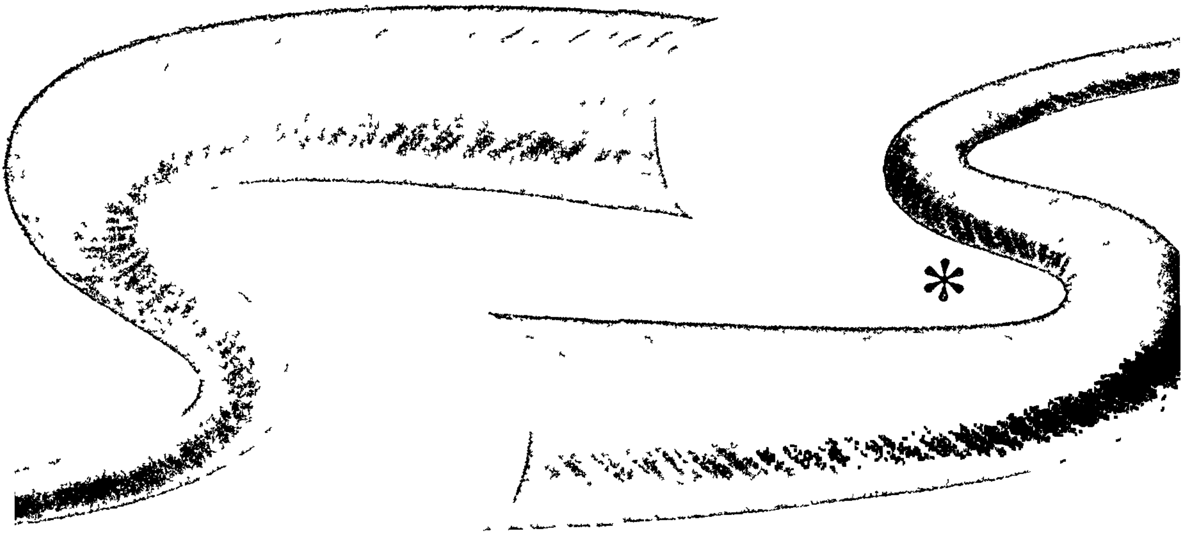

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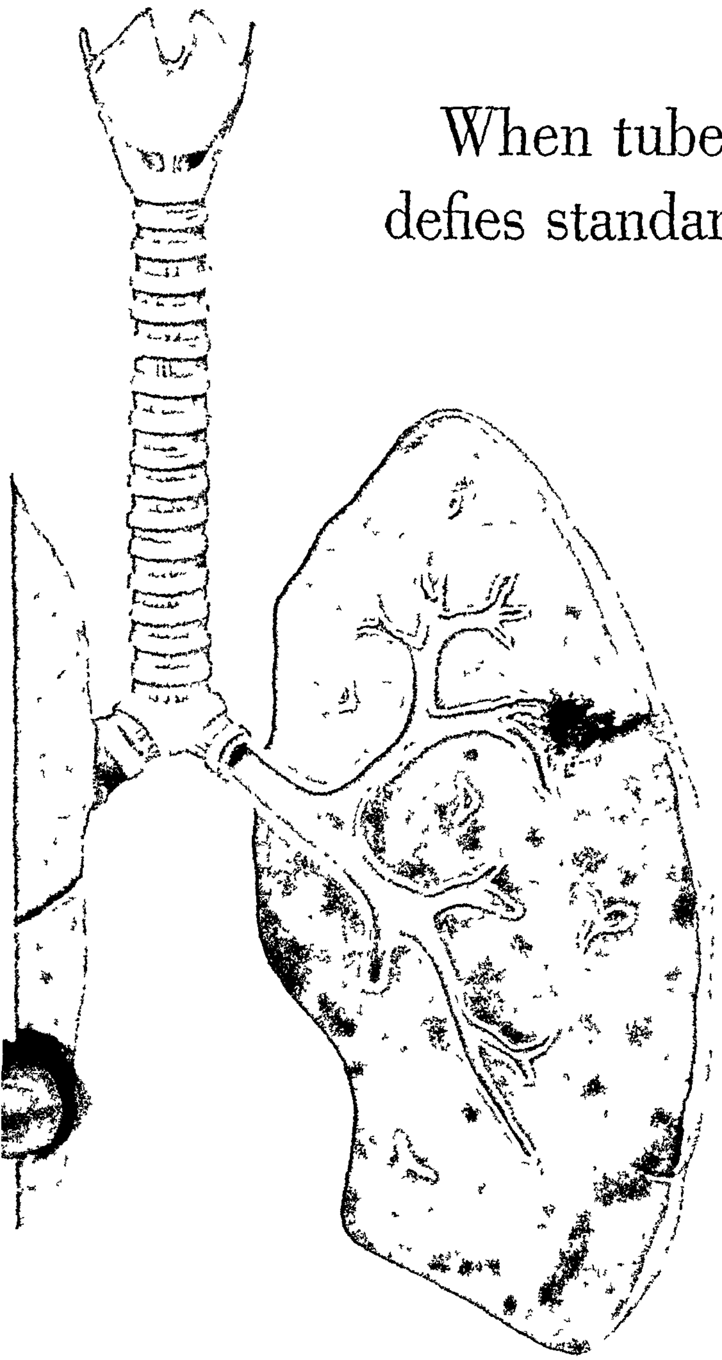

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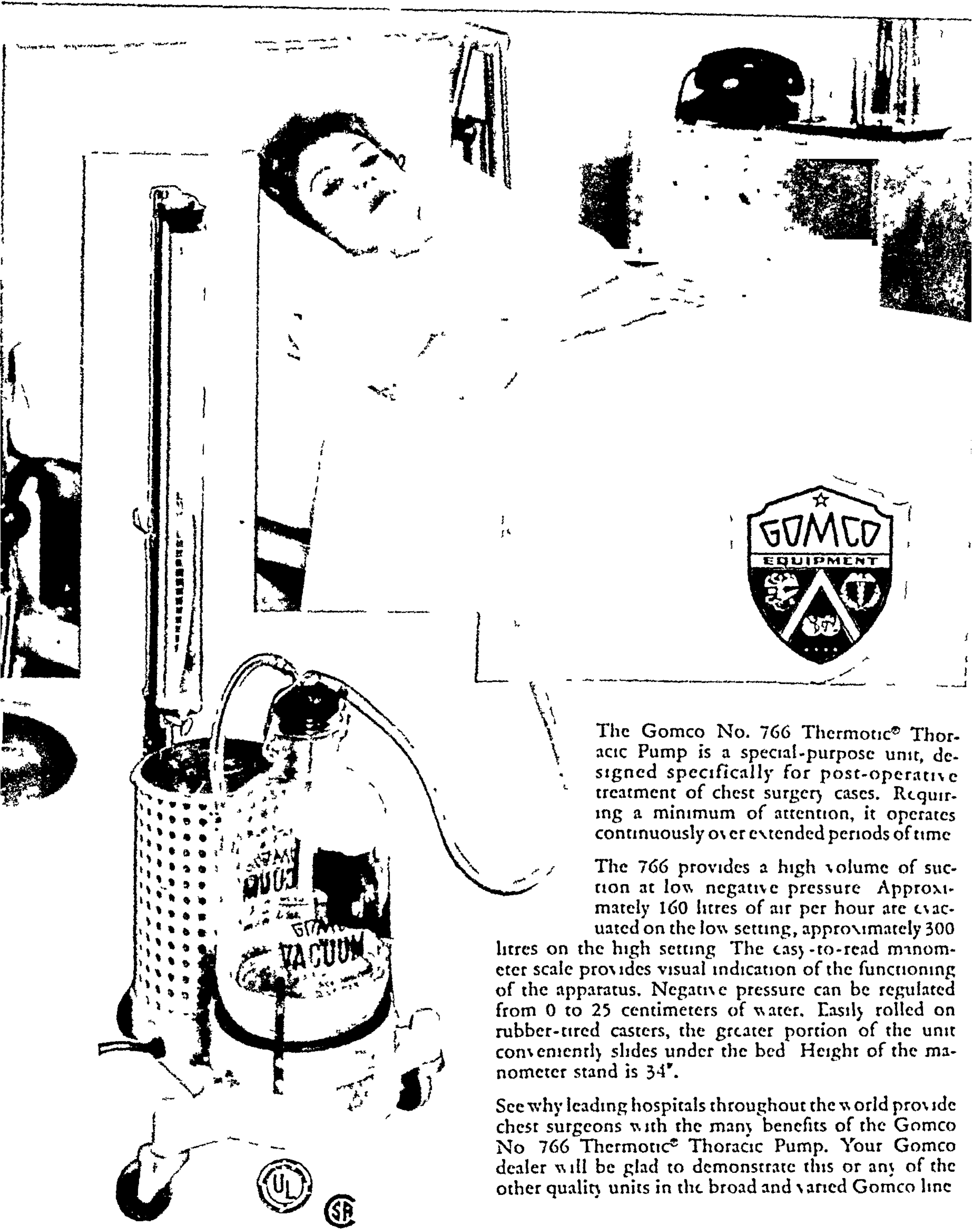

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VOLUME 39
JANUARY 1960
NUMBER 1

Original Communications

THE RELATIONSHIP OF POSTOPERATIVE ACIDOSIS TO PULMONARY AND CARDIOVASCULAR FUNCTION

George H. A. Clowes, Jr., M.D., Andrzej Alichniewicz, M.D. (by invitation), Louis R. M. Del Guercio, M.D. (by invitation), and David Gillespie, M.D. (by invitation), Cleveland, Ohio

The normal response to trauma which leads to recovery is becoming established.[29] Made up, as it is, by the intricate combination of compensatory functions of several organ systems, many variations are possible. Yet, only through knowledge of the general pattern and the degree of variation in a given patient can an estimate of his postoperative state be achieved. Following thoracic surgical operations, the system which most obviously fails is the circulation. Yet, in the majority of instances, this is secondary to respiratory inadequacy which results in chemical changes of the blood, detrimental to cardiovascular function.

From observations made upon patients subjected to pulmonary resection and other endothoracic procedures, it is the purpose of this paper to outline the pattern of the circulatory and the respiratory response during recovery in the first week. A comparison of their normal relationship with the situation existing in several patients who were hypotensive at various times during the recovery period suggests that, in man, prolonged acidosis associated with hypoxia leads, if not corrected, to sudden death from circulatory collapse.

Beecher and Murphy[2] drew attention to the profound acidosis which may develop during thoracic operations. Since that time, considerable work has been

---

From the Western Reserve University School of Medicine, Department of Surgery, Cleveland Metropolitan General Hospital, Cleveland, Ohio.

This work was supported in part by a grant from the National Institutes of Health, HC 1317-C-6.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

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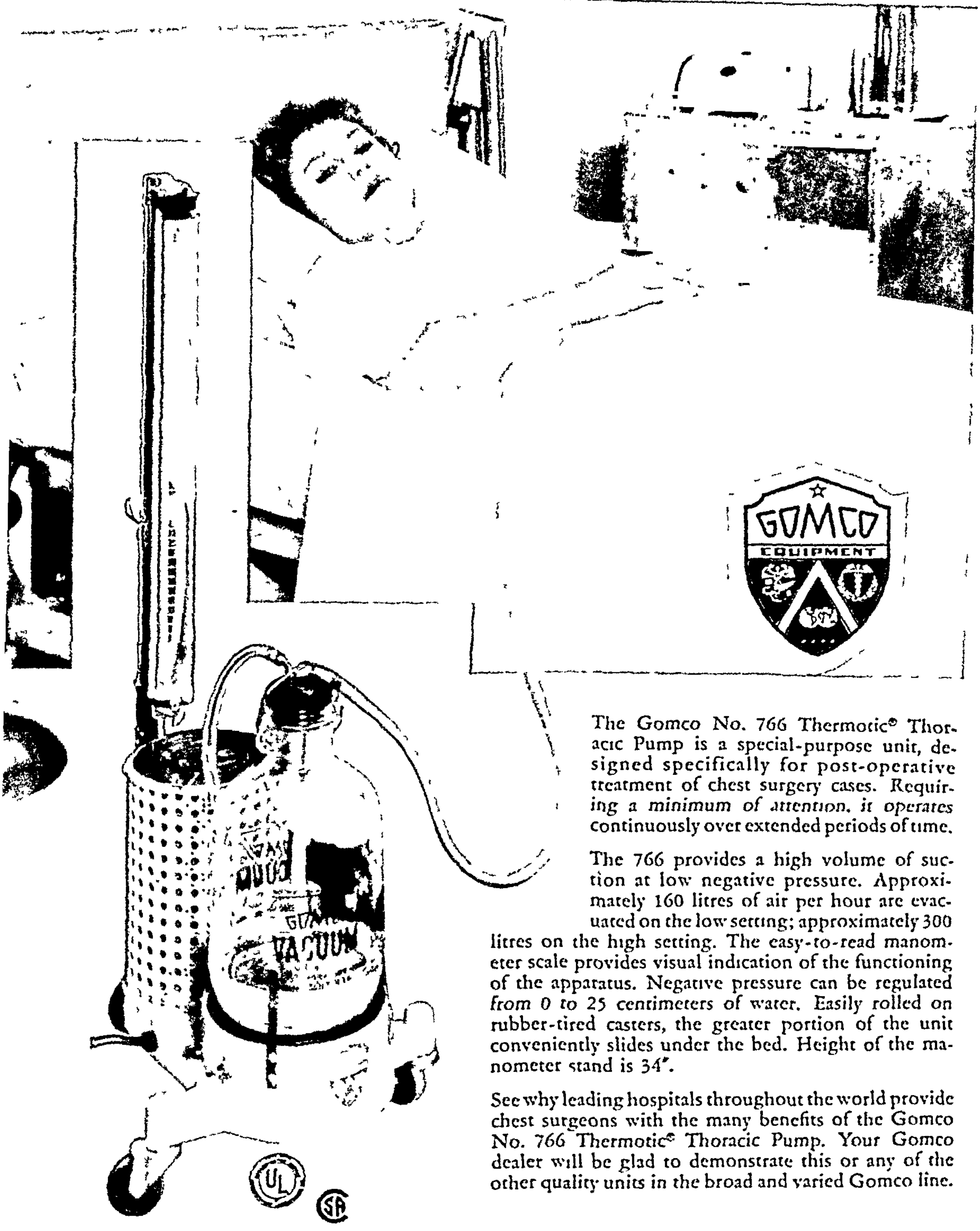

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peculiarities in fluid and electrolyte balance[31] which add another set of problems to the study of the circulatory, respiratory, and electrolyte changes caused by thoracotomy.

These patients were divided into three sections: (1) those undergoing pneumonectomy, (2) partial resection (lobectomies, segmental, and wedge resections), and (3) thoracotomy for operations upon structures other than the lung. Of the 5 patients who died, all in the postoperative period from 4 to 10 days later, 4 had undergone pneumonectomy and 1 a lobectomy.

The 10 patients who had pneumonectomies ranged in age from 37 to 64 with an average of 49 years. Five were operated upon for tuberculosis and 5 for cancer. The average maximum breathing capacity was 75 ± 12 per cent of the predicted normal and, in only two instances, was there an elevation of the walking ventilation above 11.5 L. per square meter surface area per minute.

Of the 25 patients upon whom a partial resection was performed, 16 had tuberculosis, 1 cancer, and the others a variety of infections. The average maximum breathing capacity was 78 per cent of the predicted normal. The maximum breathing capacity of 3 only was below 55 per cent. One of these subsequently died.

Ten patients underwent intrathoracic operations other than upon the lung. Of these there were two esophagectomies, three repairs of hiatus hernia, three decortications, one closure of bronchopleural fistula and thoracoplasty, and one exploration without resection. The patients' ages ranged from 40 to 66, with an average of 55. With the exception of 2 of the patients subjected to decortication, who had maximum breathing capacities below 55 per cent and vital capacities below 53 per cent of normal, the respiratory function of this group was fair, with an average maximum breathing capacity of 78 ± 10 per cent of normal.

None of the patients was hypertensive. In 3, there was evidence of previous myocardial damage or arrhythmia by electrocardiogram, or walking ventilation values above 11 L. per square meter per minute in 3. One of these subsequently suffered auricular fibrillation following lobectomy.

In all the patients reported, a combination of Pentothal (for induction only), nitrous oxide, ether, and oxygen was employed for anesthesia. In 14, Anectine was used at the time of intubation of the trachea. The majority were ventilated during thoracotomy by manual compression of the bag. A mechanical respirator was employed during all or part of the procedure in 7. Postoperative care included the use of oxygen by nasal catheter for 1 day, or more, if needed. Fluids were limited to blood replacement and approximately 1,500 c.c. of 5 per cent glucose in water during the first 24 hours. Thereafter, the patients, with the exception of those who had esophagectomy, took fluids by mouth.

All of the patients underwent study in the pulmonary function laboratory by such tests as were deemed necessary to arrive at a decision concerning the suitability and risk of the proposed operation. This included maximum breathing capacity, walking ventilation, timed vital capacity, function fluoroscopy, and bronchospirometry.

Thereafter, in the subsequent periods outlined, the respiratory observations made were on respiratory rate, tidal volume, and vital capacity. These were done with the aid of a Collins recording respirometer.* The preoperative control tests of this group were made with the patient reclining in bed under circumstances similar to those encountered postoperatively. No ventilatory measurements were made during anesthesia. Although tidal volume and respiratory rate were measured within the period of 3 to 5 hours after the operation, it was often impossible to obtain meaningful records of vital capacity due to the patient's inability to cooperate.

The hemodynamic observations included arterial blood pressure and pulse rate in all patients. The first was obtained by auscultation with a sphygmomanometer on an arm. Venous pressure determinations were made serially in 10 patients by the free fall of saline in a spinal manometer attached to the vena caval catheter. The zero line was placed at the estimated level of the right auricle.

Serial cardiac output determinations were made in 14 of the patients. The principle of measurement of cardiac output by the use of dye dilution curves recorded from the arterial system depends upon the injection of a measured amount of dye into the venous circulation as close to the heart as possible.[21] It is diluted by the blood pumped through the heart, and flow can be calculated by dividing the quantity injected by the average concentration of the dye measured in the arterial blood during the period of one circulation. The quantity of dye in the continuously sampled arterial blood can be measured photometrically,[33] and produces characteristic curves of concentration during the first and second circulation. The area of the first curve extrapolated at its termination to the base line can be converted to milligrams of dye per liter of blood by comparison with calibrations from known dilutions of the dye in samples of the patient's blood.

The dye used for injection was Indocyanine Green.†[16] Arterial blood was drawn through a densitometer (Model XC-100A‡) and the electrical output recorded on a high impedance recorder amplifier (Model 126-127§). Constant flow of arterial blood through the densitometer at 7.64 c.c. per minute was obtained with an infusion-withdrawal pump (Model 600-900‖). The quantity of dye injected ranged from 0.07 to 0.14 mg. per kilogram of body weight. A planimeter was used to calculate the area under the curve with the descending limb extrapolated to the base line. Calibration of deflection of the curve was carried out after each set of determinations by drawing heparinized samples of the patient's blood containing known dye concentrations through the densitometer at the standard rate of 7.64 c.c. per minute. From the arterial blood pressure determinations obtained with a sphygmomanometer at the time of the dye curve, mean pressure was approximated as the average of systolic and diastolic Peripheral resistance was calculated in absolute units[10] by the formula

---

*Warren E. Collins Company, Boston, Mass.

†Hynson, Westcott, and Dunning, Baltimore, Md.

‡The Waters Corporation, Rochester, Minn.

§The Sanborn Company, Cambridge, Mass.

‖Harvard Apparatus Co., Inc., Dover, Mass.

$$\text{Total Peripheral Resistance (dyne seconds/cm}^{-5}) = \frac{\text{Mean Arterial B P (mm Hg)} \times 1{,}332}{\text{Cardiac Output cm}^3\text{/sec}}$$

Arterial blood gas determinations were made upon samples obtained at each period of observation Drawn into oiled syringes sealed with mercury, the pH was measured with the Cambridge pH meter* and corrected for temperature These results were frequently checked in a pH meter heated to 38° C which showed little deviation from the calculated results †

The per cent of oxygen saturation of the blood was calculated from the nomogram of Dill,[11] employing pH and pO_2 values The latter was determined in approximately one half of the specimens by the bubble technique of Riley and his co workers[34] For the remainder, oxygen content, as measured by the method of Van Slyke and Neill,[43] was compared with capacity to arrive at a value for the per cent of saturation When both were available they were checked against each other In general, there was close agreement

The carbon dioxide tension was calculated employing the nomogram of Singer and Hastings[35] which requires knowledge of the hematocrit, pH and carbon dioxide content obtained from Van Slyke analysis[43] More than one half of these values was checked again with close agreement by carbon dioxide tensions measured by the bubble technique[34] In 11 instances where there was a discrepancy, the values obtained by the latter method were accepted

Blood electrolyte values were obtained from the heparinized arterial samples taken at the times the respiratory and other tests were carried out Sodium and potassium concentrations were measured with the Baird‡ flame photometer

For the determination of ionized calcium, plasma from arterial blood collected under oil was subjected to ultrafiltration in a modification of the Lavietes cell[21] This is so arranged that the filtrate is separated from the cellophane membrane by a layer of mercury to avoid the interference of dialysis Both total and filtrable calcium concentrations were determined by the EDTA titration method of Carr and Frank[6] In order to arrive at a value for ionized calcium from the nomogram of McLean and Hastings for the dissociation of calcium citrate,[22] it is necessary to know the concentration of citric acid in the filtrate which was obtained by the technique of Ettinger, Goldbaum, and Smith[12]

Plasma lactate values were measured by the colorimetric method of Barker and Summersen[1] Inorganic phosphorus and protein levels in the plasma were obtained by the methods respectively, of Fiske and Subbarow[13] and Weichselbaum[44]

RESULTS

Data concerning the circulation, respiration, arterial blood gas and pH, and the blood electrolyte pattern of the patients who survived thoracotomy are

---

*Cambridge Instrument Company Cambridge Mass

†Courtesy Dr Byron Bloor

‡The Baird Company Cambridge Mass

TABLE I. CIRCULATORY VALUES AND STANDARD DEVIATIONS OF SURVIVING PATIENTS

NUMBER	OPERATION	PREOP.	ANESTHESIA	OPERATION	POSTOPERATIVE PERIOD				
					3-5 HR.	1 DAY	2 DAYS	3-4 DAYS	1 WEEK
	Pneumonectomy								
7	Pulse rate	85 ± 7	95 ± 10	102 ± 10	94 ± 18	94 ± 20	91 ± 15	94 ± 12	92 ± 8
7	Arterial blood pressure	121 ± 12 $\overline{72}$ $\overline{6}$	116 ± 18 $\overline{80}$ $\overline{10}$	102 ± 24 $\overline{60}$ $\overline{10}$	104 ± 12 $\overline{67}$ $\overline{8}$	117 ± 10 $\overline{78}$ $\overline{7}$	112 ± 10 $\overline{70}$ $\overline{6}$	117 ± 12 $\overline{70}$ $\overline{7}$	120 ± 10 $\overline{73}$ $\overline{5}$
2	Cardiac output (% diff. from preop.)	4.6 ± 1.0 L./min.	−10 ± 8%	−32 ± 12%		+8 ± 5%	+22 ± 14%		+24 ± 11%
	Partial Resection								
23	Pulse rate	84 ± 8	100 ± 15	99 ± 10	101 ± 16	103 ± 18	111 ± 16	103 ± 10	95 ± 8
23	Arterial blood pressure	118 ± 14 $\overline{74}$ $\overline{7}$	122 ± 12 $\overline{82}$ $\overline{10}$	112 ± 26 $\overline{68}$ $\overline{12}$	109 ± 22 $\overline{70}$ $\overline{10}$	121 ± 16 $\overline{73}$ $\overline{5}$	118 ± 12 $\overline{75}$ $\overline{6}$	120 ± 10 $\overline{75}$ $\overline{5}$	121 ± 10 $\overline{77}$ $\overline{5}$
9	Cardiac output (% diff. from preop.)	5.9 ± 0.8 L./min.	−11.2 ± 13%	−33 ± 10%	+7.1 ± 4.1%	+9.3 ± 8.5%	+32 ± 28%		+16 ± 12%
	Other Thoracotomies								
10	Pulse rate	89 ± 5	100 ± 5	100 ± 7	100 ± 15	95 ± 14	97 ± 15	96 ± 11	93 ± 12
10	Arterial blood pressure	125 ± 12 $\overline{78}$ $\overline{4}$	115 ± 11 $\overline{78}$ $\overline{3}$	110 ± 26 $\overline{65}$ $\overline{8}$	120 ± 23 $\overline{74}$ $\overline{11}$	125 ± 20 $\overline{81}$ $\overline{3}$	126 ± 18 $\overline{80}$ $\overline{5}$	125 ± 14 $\overline{78}$ $\overline{4}$	125 ± 14 $\overline{79}$ $\overline{5}$
4	Cardiac output (% diff. from preop.)	5.2 ± 1.1 L./min.	−9 ± 15%	−30 ± 13%	+57 ± 29%	+45 ± 29%	+47 ± 40%		+21 ± 15%

given with their standard deviations in Tables I, II, III, and IV. To permit comparison of the effects produced at different stages of recovery by the three types of operative procedure, each table is divided to present separately the data from pneumonectomies, partial resections, and other intrathoracic operations. As may be seen from examination of the standard deviations, little significant difference exists in the observations obtained from the three groups. Attention will be drawn to those situations in which important variations do occur. For convenience, then, the average values for surviving patients are given in Figs. 1, 2, 3, and 4.

Five patients died postoperatively at times ranging from 4 to 10 days postoperatively. In each instance this followed respiratory insufficiency from pneumonia. The data from these patients are presented in Table V. The course of a patient typical of those in this group who died is given in Fig. 5.

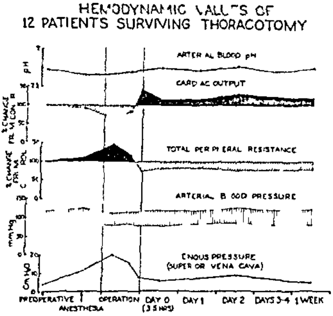

Fig. 1

Circulatory Observations.—Little difference in blood pressure or pulse rate (Table I) existed in the response of the three surviving groups to the operation. Adequate data from serial observations are available on the cardiac output of 14 patients. The average preoperative cardiac output by the dye dilution technique was 5.33 L. per minute with a standard deviation of ±0.96 liter.

Although there was only a moderate and statistically insignificant depression of blood pressure during the induction of anesthesia and the operation, the average cardiac output fell 9 ± 5.9 per cent in the first period, and later in the operation to −32 ± 10.5 per cent from the control level. The latter is significant ($p < 0.02$). At this time, the average total peripheral resistance rose to 45 ± 13.4 per cent above the preoperative value of 1,857 dynes cm./sec.[5] Later in the operation the cardiac output returned toward normal, being 16.2 ± 2.56 per cent below the preoperative level. The blood pressure was also returned to nearly normal values giving a calculated peripheral resistance 16 ± 9.8 per cent above normal.

The vena caval pressure promptly rose from 5.8 ± 1.5 cm. H_2O during the induction of anesthesia and intubation to 14.5 ± 6.2 cm. Throughout the re-

TABLE II. VENTILATION AND STANDARD DEVIATIONS OF SURVIVING PATIENTS

NUMBER	OPERATION	PREOP.	ANESTHESIA	OPERATION	POSTOPERATIVE PERIOD				
					3-5 HR.	1 DAY	2 DAYS	3-4 DAYS	1 WEEK
	Pneumonectomy								
5	Tidal volume (L./min.)	0.48 ± .10 (7)			0.40 ± .06	0.45 ± .07	0.47 ± .08	0.50 ± .10	0.52 ± .09
7	Respiratory rate	22 ± 2			25 ± 4	24 ± 4	21 ± 3	25 ± 4	22 ± 4
5	Vital capacity (L./min.)	2.81 ± .34 (7)				1.32 ± .16	1.34 ± .19	1.43 ± .24	1.65 ± .22
	(% normal)	69% ± 9% (7)				32%	34%	37%	41%
	Partial Resection								
8	Tidal volume (L./min.)	0.45 ± .07 (23)			0.34 ± .08	0.37 ± .06	0.40 ± .07	0.47 ± .06	0.52 ± .08
23	Respiratory rate	20 ± 2			26 ± 4	26 ± 5	26 ± 4	25 ± 4	22 ± 5
8	Vital capacity (L./min.)	3.12 ± .72 (23)				1.09 ± .31	1.12 ± .27	1.35 ± .25	1.35 ± .26
	(% normal)	81% ± 13%				28%	29%	36%	36%
	Other Thoracotomies								
4	Tidal volume (L./min.)	0.46 ± .13 (10)			0.40 ± .10	0.41 ± .09	0.39 ± .07	0.38 ± .07	0.45 ± .11
10	Respiratory rate	19 ± 3			27 ± 3	25 ± 5	26 ± 4	24 ± 4	23 ± 4
4	Vital capacity (L./min.)	2.78 ± .68 (10)				0.98 ± .28	1.13 ± .26	1.24 ± .38	1.44 ± .36
	(% normal)	73% ± 12% (10)				27%	30%	33%	38%

mainder of the operation it remained elevated between 15 and 18 cm H_2O on the average, with a greatest standard deviation of ±4 82 Following extubation it returned to near preoperative levels where it remained through the convalescent period

At the termination of the operation when the tube was removed from the larynx a slight fall in blood pressure took place in all patients to an average of 105/64 mm Hg, but cardiac output increased in all The average value was +40 2 ± 36 per cent above the preoperative level The large standard deviation is due to the great rise in 2 patients to +210 and +232 per cent At this time, peripheral resistance was found to be decreased 26 ± 7 7 per cent under the resting value Up to 1 week, cardiac output remained elevated, the greatest being on the second postoperative day when it was 31 ± 23 9 per cent over the preoperative level By the end of a week it had returned to 19 6 ± 16 per cent

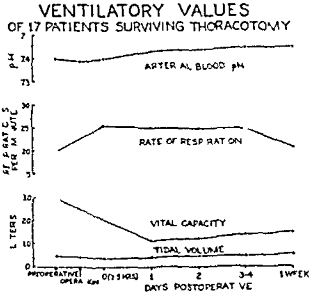

Fig 2

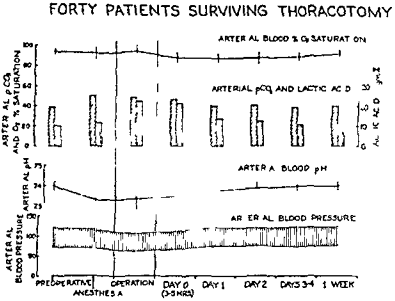

Fig 3

The blood pressure and pulse rate of patients who died postoperatively behaved in most respects in a fashion similar to those of the survivors until 2 to 3 days prior to death As shown in Table V, the pulse rate was significantly elevated above that of the survivors at a corresponding time More important the mean of the blood pressures was somewhat lower 2 days before death and significantly lower on the day before (94/52 ± 8/12 mm Hg) and on the day of death (85/48 ± 7/20 mm Hg) It was notable that blood pressure tended to change abruptly upward and downward during the last 2 days, as measured from hour to hour In general, the pulse rate varied inversely as the blood pressure in this period No consecutive data are available concerning cardiac output in this group

Ventilation—The patients who survived pneumonectomy, partial resection of lung, and other intrathoracic procedures were comparable preoperatively and showed no significant differences of respiratory rate in their tidal volumes which averaged 460 ± 90 c c, or the vital capacities which averaged 76 ± 12 per cent of the predicted normal As shown in Fig 2, there was a moderate reduction in tidal volume with an increase of respiratory rate in the early postoperative course During the first day after the operation, the mean tidal volume of

TABLE III. BLOOD GAS VALUES AND STANDARD DEVIATIONS OF SURVIVING PATIENTS

NUMBER	OPERATION	PREOP.	ANESTHESIA	OPERATION	POSTOPERATIVE PERIOD				
					3-5 HR.	1 DAY	2 DAYS	3-4 DAYS	1 WEEK
7	*Pneumonectomy*								
	pCO_2	38 ± 4	54 ± 16	49 ± 10	41 ± 6	42 ± 8	41 ± 4	38 ± 4	40 ± 4
	pH	7.38 ± .02	7.32 ± .04	7.34 ± .06	7.40 ± .03	7.41 ± .02	7.41 ± .03	7.39 ± .03	7.40 ± .02
	% O_2 saturation	94 ± 4	93 ± 9	94 ± 4	93 ± 2	91 ± 5	92 ± 3	91 ± 3	93 ± 2
23	*Partial Resection*								
	pCO_2	40 ± 4	49 ± 7	51 ± 7	48 ± 3	42 ± 3	42 ± 2	41 ± 2	38 ± 2
	pH	7.40 ± .02	7.33 ± .05	7.32 ± .05	7.33 ± .05	7.39 ± .03	7.40 ± .01	7.40 ± .02	7.41 ± .01
	% O_2 saturation	93 ± 4	90 ± 6	95 ± 5	89 ± 5	86 ± 5	84 ± 6	89 ± 3	94 ± 3
10	*Other Thoracotomies*								
	pCO_2	38 ± 6	47 ± 4	48 ± 7	46 ± 4	39 ± 3	38 ± 2	36 ± 4	38 ± 2
	pH	7.40 ± .03	7.34 ± .04	7.35 ± .04	7.35 ± .02	7.38 ± .02	7.39 ± .03	7.42 ± .02	7.40 ± .02
	% O_2 saturation	94 ± 2	96 ± 2	97 ± 2	87 ± 6	88 ± 4	89 ± 6	91 ± 3	92 ± 5

those who had lobectomies (370 ± 60 c c) remained below that of the other two groups The pneumonectomies averaged 450 ± 70 c c In the majority, tidal volume had returned to normal by the fourth day and in all by the end of a week

Vital capacity on the day after the operation fell significantly in all cases to levels averaging 28 per cent of the predicted normal This reduced the average respiratory reserve in the three groups to between 24 and 37 per cent of what it had been before the operation As may be seen from Table II this reduction of vital capacity was least among the postoperative pneumonectomies By the end of 1 week, the average vital capacity reached a level of 51 per cent of the preoperative value or 38 per cent of normal The patients who died did not show any statistically significant difference in respiration from the survivors although tidal volume tended to be lower

Arterial Blood Gas and Hydrogen Ion Concentration —Preoperatively there were 5 patients with arterial blood oxygen saturations below 90 per cent These ranged from 78 to 89 per cent Of these, 1 had a moderately elevated pCO_2 Otherwise carbon dioxide tension was normal in all of the patients

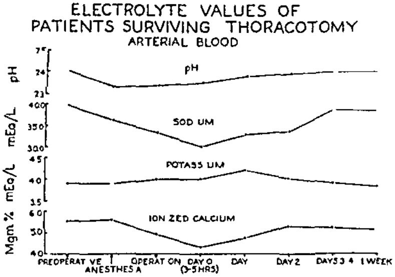

Fig 4

During the induction of anesthesia, 19 patients were found to be acidotic Ten of these were grossly so, with arterial pH values below 7 30 Subsequently in the course of the thoracotomy, acidosis was present in 21, 5 of them having pH values between 7 2 and 7 3 The pH of 3 was below 7 2 Three to 5 hours following the operation, acidosis was observed in 12 patients, although 5 of these had not been acidotic during the operation

In each case, the acidosis was related to CO_2 retention Carbon dioxide tension on the average, as shown in Table III, was above or at the upper limits of normal, with large standard deviations indicating the wide range of observations during these periods

One case in particular is reported in this connection

E R (U 83057), a 17 year old Negro man, was admitted to Lowman Pavilion with a diagnosis of cavitary tuberculosis of the right upper lobe, 5 months prior to operation He was treated with isoniazid and para aminosalicylic acid The vital capacity was 61 cent and maximum breathing capacity 78 per cent of predicted normal. Blood gas studies disclosed the arterial pH to be 7.40; pCO_2, 44; and oxygen saturation, 93 per cent. Blood chemical determinations were also within normal limits. The patient was in good condition and considered a satisfactory candidate for right upper lobectomy. This was undertaken on Sept. 11, 1958, and the operation was accomplished without difficulty in approximately 3 hours and 20 minutes. However, it was noted that the patient breathed at times with great effort. The blood pressure dropped from the preoperative level of 120/80 to 85/60 mm. Hg during induction and subsequently returned to 125/90 from which it gradually fell to 102/82 by the end of the procedure. As the chest was being closed, it was reported that the arterial pCO_2 in the blood sample, drawn an hour before, was 145 mm. Hg and the pH 6.91 while oxygen saturation was 93 per cent. Investigation disclosed that through an oversight, the CO_2 absorbing cannister had not been placed in the anesthesia machine. By slowly diluting the bag mixture with oxygen to avoid a sudden shift to pure oxygen, the pCO_2 was reduced. Within an hour, the arterial carbon dioxide tension was 62 mm. Hg while the pH was brought up to 7.21. The blood pressure fell to 72/50 mm. Hg. A gram of calcium chloride administered intravenously promptly restored it to 105/74 mm. Hg. During the subsequent 4 hours, the arterial pCO_2 was reduced to 36 mm. Hg, although the pH could not be made to rise, above 7.22. The blood lactic acid was 52 mg. per cent. The potassium rose to 5.9 mEq./L. while the ionized calcium dropped to 0.7 mM./L. At this time the patient was anuric, but urinary output started 4 hours postoperatively and quickly increased in volume. Within the next 3 hours, 750 c.c. was excreted. Concurrently with the onset of diuresis, the arterial pH rose slowly to 7.38. Except for some lassitude and a headache for 2 days, the patient made an otherwise uneventful recovery.

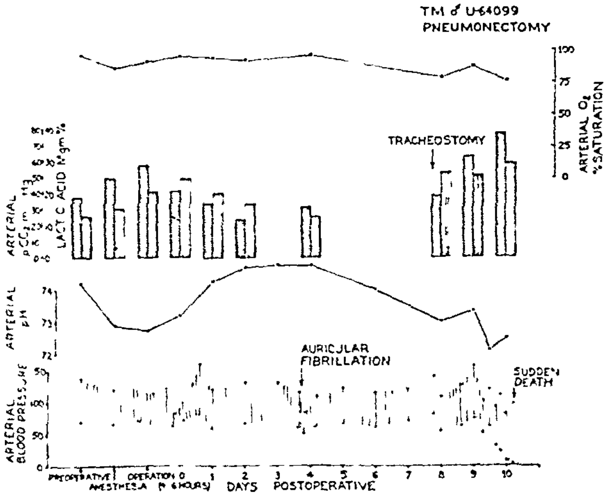

Fig. 5.

Throughout the postoperative period, the oxygen content of the arterial blood was maintained near normal in all but 2 of the patients surviving pneumonectomy. In these, it was depressed only for a single day during a critical period. On the other hand, as shown in Table III, there was a significant fall of hemoglobin oxygen saturation among the patients who underwent lobectomy. This was most noticeable on the second day postoperatively, when the average oxygen saturation had fallen to 84 ± 6 per cent from 93 ± 4 per cent ($p < 0.05$). This trend was less marked in the third group of patients who underwent operations on structure other than the lung, but was particularly noticeable among the 3 patients who underwent decortication On the second postoperative day the hemoglobins were 81, 84, and 85 per cent saturated from preoperative control levels which ranged from 87 to 93 per cent saturated

The data in Table V suggest that the blood gas values of the patients who died were not significantly different from the survivors during the operation and for 2 days thereafter But when the available data for the 2 days preceding death are examined, it will be seen that, despite efforts to improve respiration by aspiration, tracheostomy, assisted ventilation, and other measures, there was a progressive and significant fall of oxygen saturation to an average of 76 ± 8 per cent on the day preceding death The arterial pH also fell to 7 26 In 3 patients values between 7 12 and 7 28 were recorded just before death The pCO_2 rose reaching a level above 60 mm Hg in the 3 patients from whom blood was drawn on the day prior to death An example of this is shown in Fig 5

Blood Electrolytes, Lactate, and Phosphate—Among the surviving patients there is little difference in the pattern of blood electrolyte response A significant fall in sodium took place which was most pronounced on the afternoon of the operation and the following day It was not unusual to find the plasma sodium below 128 mEq L

TABLE IV BLOOD CHEMISTRY AND STANDARD DEVIATIONS OF SURVIVING PATIENTS

					POST OPERATIVE PERIOD				
NUMBER	OPERATION	PREOP	ANESTHESIA	OPERATION	3 5 HR	1 DAY	2 DAYS	3 4 DAYS	1 WEEK
	Pneumonectomy								
5	Sodium (mEq /L)	137 ± 6	134 ± 6	132 ± 5	135 ± 5	131 ± 3	133 ± 5	134 ± 4	137 ± 5
7	Potassium (mEq /L)	3 9 ± 4	3 9 ± 4	4 0 ± 3	4 0 ± 4	3 7 ± 3	3 7 ± 3	3 9 ± 5	3 8 ± 4
6	Ion calcium (mg %)	5 8 ± 6	6 5 ± 5	5 0 ± 5	4 6 ± 4	5 0 ± 5	5 2 ± 4	5 3 ± 4	5 2 ± 4
6	Lactate (mg %)	12 ± 4	16 ± 5	27 ± 5	17 ± 6	20 ± 4	13 ± 5	14 ± 5	10 ± 4
	Partial Resection								
20	Sodium (mEq /L)	141 ± 6	139 ± 7	133 ± 4	131 ± 5	135 ± 6	135 ± 5	140 ± 7	139 ± 4
23	Potassium (mEq /L)	3 9 ± 3	4 1 ± 5	3 9 ± 4	3 9 ± 5	4 4 ± 3	4 1 ± 3	3 9 ± 3	3 9 ± 3
23	Ion calcium (mg %)	5 3 ± 4	5 5 ± 2	4 9 ± 6	4 1 ± 4	4 5 ± 2	5 3 ± 3	5 2 ± 3	5 1 ± 4
23	Lactate (mg %)	10 ± 4	17 ± 6	25 ± 7	26 ± 5	17 ± 6	16 ± 5	11 ± 5	9 ± 4
	Other Thoracotomies								
9	Sodium (mEq /L)	138 ± 7	132 ± 5	135 ± 7	131 ± 6	129 ± 6	131 ± 7	138 ± 8	138 ± 6
9	Potassium (mEq /L)	3 8 ± 3	3 6 ± 2	4 0 ± 3	4 1 ± 2	4 0 ± 2	4 0 ± 2	4 0 ± 3	3 7 ± 4
8	Ion calcium (mg %)	6 0 ± 5	5 0 ± 3	4 6 ± 3	4 6 ± 2	4 9 ± 3	5 3 ± 4	5 6 ± 3	
8	Lactate (mg %)	11 ± 3	14 ± 5	21 ± 6	24 ± 3	19 ± 3	13 ± 3	14 ± 4	10 ± 3

The potassium levels were either not changed or only very slightly elevated on the first and second days postoperatively These differences were not statistically significant

The *ionized calcium* levels *were depressed consistently and significantly* ($p > 0\ 02$) *in all groups on the afternoon of operation to a level 21 per cent* below that found preoperatively In general, these had returned to their control values by the second day

The average concentration preoperatively of inorganic phosphate was 3.3 ± 0.5 mg. per cent which rose to a peak during the operation and in the immediate postoperative period to 4.5 ± 0.6 mg. per cent. This returned in the course of the next 2 days to the preoperative value. The blood lactate followed a similar pattern starting at 10.7 ± 4 mg. per cent and rising on the average to 24.4 ± 6. This ordinarily required 3 days to drop to normal. In those patients who were hypoxic or hypotensive, lactate values as high as 57 mg. per cent were seen.

Summaries of the histories of surviving patients who developed transient postoperative pulmonary insufficiency and hypotension follow.

W. B. (U-80326), a 62-year-old white man who underwent an uneventful pneumonectomy for tuberculosis on April 19, 1956, had a preoperative vital capacity of 69 per cent and a maximum breathing capacity of 80 per cent. In other respects also he was considered a satisfactory candidate for the operation. On the morning after the operation, he continued to be hypotensive (B.P. 80/58). Both physical examination and x-ray disclosed atelectasis of the remaining lower lobe. The arterial pH which had been normal before and during the operation was 7.29. The carbon dioxide tension had risen to 65 mm. Hg and the oxygen saturation was 82 per cent. Lactic acid and potassium were both moderately elevated, the latter to 5.8 mEq./L. Bronchoscopy was performed with the removal of a mucus plug giving good aeration of the lobe. Blood pressure promptly returned to 130/92 mm. Hg. An arterial blood sample drawn a few hours later revealed that pH, pCO_2, and oxygen saturation had become normal again. He made an uneventful convalescence thereafter.

T. C. (U-45764), a 48-year-old white man, was admitted for cavitary tuberculosis involving the right upper and middle lobes. The preoperative arterial pH was 7.36 with a
$_2$ of 40 mm. Hg and 92 per cent oxygen saturation. Vital capacity was 81 per cent and
maximum breathing capacity 69 per cent of normal. On April 30, 1957, he underwent a
upper and middle lobectomy and made a satisfactory recovery that afternoon. The next
g his blood pressure was found to be 78/52 and he appeared dyspneic and cyanotic,
te the administration of oxygen by nasal catheter. The arterial pCO_2 was 67 mm. Hg
the pH 7.28. The hemoglobin was 79 per cent saturated. Blood lactate had risen to
ng. per cent. Calcium and potassium levels were normal. Bronchoscopy was performed
to relieve a left lower lobe atelectasis. The blood pressure rose to 120/68 mm. Hg with a decrease of pulse rate from 130 to 116. A blood sample the next day gave a pH of 7.38 and blood gas values within normal limits. The lactate had fallen to 18 mg. per cent.

A. L. (U-63478), a 42-year-old white woman, was admitted 13 months preoperatively for pulmonary tuberculosis. Preoperative pulmonary function studies disclosed that the vital capacity was 57 per cent and the maximum breathing capacity was 64 per cent of normal. The left lung was performing 28 per cent of the ventilation and 21 per cent of the oxygen uptake. Blood gas and electrolyte values were normal. On Jan. 9, 1957, she underwent a left pneumonectomy with essentially an uneventful convalescence until the fifth day when it was discovered that she had developed pneumonia in the right lung. On the sixth day, despite efforts at coughing and aspiration, many ronchi were heard. The blood pressure gradually fell from 110/72 to 92/64 mm. Hg with fluctuations up and down. A blood sample disclosed the arterial pH to be 7.30 whereas the pCO_2 was 67 mm. Hg. The blood was 82 per cent oxygen saturated. A tracheostomy was performed for suction and assisted respiration. Within 6 hours, the blood pressure had risen to 135/85. The next day the arterial pH was 7.37 and the pCO_2 44 mm. Hg. Oxygen saturation had risen to 89 per cent. The electrolytes were all normal except for the sodium which was 129 mEq./L. She subsequently made an uneventful recovery.

Two case summaries of patients who died postoperatively are presented here as typical examples of the type of respiratory problems which were followed by death

C V (U 33193), a 57 year old man, who entered for his fourth admission because of severe dyspnea of 6 months' duration He had arrested tuberculosis and had developed emphysematous cysts of both bases, most marked in the right lower lobe This seriously compressed the remaining lung tissue The arterial blood had a pH of 7 41 with a pCO_2 of 2 mm Hg The hemoglobin was 78 per cent saturated with oxygen Blood pressure was 10/68 mm Hg Despite a vital capacity of 40 per cent and maximum breathing capacity t 35 per cent, a right lower lobectomy and tracheostomy were performed on Feb 12, 1958, n an attempt to improve the respiratory capacity Postoperatively, he developed paralytic us and required gastric suction The arterial oxygen saturation did not change, but the pCO rose to 79 mm Hg with an accompanying depression of pH to 7 20 on the afternoon f the operation Pulse was near 110 and blood pressure 100/76 The next day, oxygen saturation was 69 per cent but pCO_2 had fallen to 52 mm Hg, with a pH of 7 37 On the third day, he appeared to be lethargic although the nail beds were pink Bronchial breathing was present in the right upper chest, and x ray studies suggested bronchopneumonia despite active aspiration of the trachea At that time, the arterial pH was 7 32 and urine output had decreased to 22 c c per hour The plasma sodium had fallen to 129 from 148 mEq /L The potassium had risen to 5 9 mEq /L The blood pressure varied between 120/90 and 90/50 mm Hg Temperature was 40° C per rectum On the morning of the fourth day, the situation was essentially unchanged, despite the use of assisted respiration through the tracheostomy with the Bennett valve At this time, the pH of the arterial blood was 7 22 and the pCO 73 mm Hg The oxygen saturation was 68 per cent His blood pressure remained near 90/68 mm Hg, with a pulse rate of 120 Shortly thereafter he vomited became cyanotic, and suddenly died

T M (U 64099) (see Fig 5), a 54 year old Negro man, was admitted because of a cough of 1 month's duration X rays showed atelectasis of the left upper lobe The vital capacity was 92 per cent and maximum breathing capacity 84 per cent of normal Preoperative blood studies, including pH, pCO, oxygen saturation potassium, and sodium, were normal A diagnosis of pulmonary carcinoma was made, and a pneumonectomy was performed on Aug 6, 1958 His postoperative course is illustrated in Fig 5 Except for continued intrapleural bleeding postoperatively, requiring four additional blood transfusions, the course was *uncomplicated* until the seventh *postoperative day* when respiration became difficult due to secretions Auricular fibrillation occurred and the rate was controlled with digitalis A tracheostomy was performed with some improvement However, his downward course continued He died on the tenth day with a sudden fall of blood pressure At autopsy a cerebellopontine metastasis was found

DISCUSSION

The response of the circulation to thoracic surgical operations as observed in 14 surviving patients is shown in Fig 1 The number of observations is too small to permit comparison in the various types of operations Yet, the circulatory alterations fell into the same general pattern The anesthetic and operative procedure produced a depression of cardiac output (−35 ± 5 2 per cent) with increased total peripheral resistance (+45 ± 13 5 per cent) Postoperatively this was followed by an immediate rise of output, acutely stimulated at the time of extubation This was accompanied by a decrease of resistance (−26 ± 7 8 per cent) Throughout the remainder of the recovery period, the ituation was unchanged. On the average, the cardiac output was at its greatest +31 ± 13.9 per cent) on the second postoperative day. At that time, the eripheral resistance was -25 ± 3 per cent of the preoperative level. Toward he end of the week, both tended to approach normal values.

The observed decrease in cardiac output and the rise of central venous ressure during anesthesia are well known and have been shown to be indeendent of either acidosis or hypoxia.[14, 35] Depression of the myocardium by he anesthetic agent or an increase in pulmonary vascular resistance has been uggested as a cause.[25] The further depression of cardiac output during the peration to values as low as 51 per cent of the resting output may well have been the result of blood loss, yet it is probable that this also was related to a hange in cardiac function. Calculation of stroke volume shows that following the induction of anesthesia it fell from an average preoperative level of 59 ± 8 c.c. to 52 ± 4 c.c. Later in the operation, the average stroke volume was 34 ± 4 c.c. which was a significant change. Possibly this is related to the fall of pH which has been so commonly found during such procedures.[2] Jerusalem and Starling[24] observed that the cardiac dilation caused by carbon dioxide retention "affected the systolic more than the diastolic volume, so that the ventricular output is diminished."

It is likely that the marked rise in cardiac output, observed following anesthesia as the patients were extubated, was the result of a stimulus resulting in a release of epinephrine. This is suggested by the marked rise of pulse rate. Possibly it is also provoked by increased circulatory demands during coughing and struggling.

During the days succeeding the operation, the increase in circulation was met by a rise of pulse rate which averaged 117 ± 5 in these patients rather than an increase of stroke volume. The latter (65 ± 7 c.c.) remained near the preoperative value of 59 ± 8 c.c. This observation of augmented output in the recovery period differs from that of Snyder[10] who found a fall of 41 per cent in 8 patients following abdominal operations. In his experience, 5 days were required for return to normal. It may be argued that the greater output at this time was the result of mild hypoxia which is a well-established cause for epinephrine release.[5] Gellhorn's[17] observations on man subjected to mild hypoxia suggested a rise of cardiac output. In this connection it is of interest that the least tachycardia was observed in the patients who had had pneumonectomies. They also showed the least hemoglobin oxygen desaturation. Furthermore, Stead[41] observed an increase of the metabolic rate 1 day following lobectomy and thoracoplasty amounting to 128 per cent of the preoperative value. This might well be expected to result in elevation of the circulatory flow.

Both Martin and Stead[28] and Hood and Beall[23] found that a large proportion of patients were underventilating within the first hour after the completion of thoracic operations, with a tendency toward a fall in arterial pH. At the time when measurements were made on this series of patients (3 to 5 hours after surgery), the tidal volumes were only slightly depressed and the pH values were within the normal range in almost all of the patients. The exceptions to this were among those who had had lobectomies and who showed a significant depression of tidal volume with a marked increase in respiration However, by employing Fowler's factor for normal anatomic dead space,[15] it appears that alveolar ventilation was only slightly depressed in the great proportion of patients, the average being −16 ± 12 per cent below the preoperative resting level among the survivors

On the following day, the data in Table II indicate that tidal volumes were not significantly below normal and the respiratory rates were moderately elevated Although subject to some error, by the means used to calculate them, the average of alveolar ventilation was only slightly depressed (−10 ± 12 per cent), not significantly so This is in contrast to Stead's observation which showed a depression of 35 per cent[41] However, his patients had been subjected to a combined pulmonary resection and thoracoplasty, making respiration more difficult Fig 2 shows how these nearly normal tidal volumes were maintained despite a marked reduction in the vital capacity and respiratory reserve

It is impressive how exactly the pH and pCO_2 of the blood were maintained within the narrow margins considered to be normal from the first postoperative day onward in the surviving 40 patients The only exceptions were the 3 patients whose histories are presented and who developed problems of ventilation and inability to keep the arterial pCO_2 below 48 mm Hg for relatively short periods of time

Although pCO_2 was maintained normally, there was a moderate oxygen desaturation in the arterial blood of almost all the patients The data in Table III suggest that this was significantly greater among those who underwent lobectomy and may be related to edema caused by trauma to the lung left in situ This phenomenon was also noted to a lesser extent in those patients who underwent operations upon other structures within the chest Ordinarily, this was most pronounced on the second day when a hazy ground-glass appearance of the lung on the side of operation was seen by x-ray Usually resolution took place within 4 days and was accompanied by a return toward normal of the hemoglobin oxygen saturation Maier[27] noted this and suggested that blood stasis in the lung might be a factor in producing postoperative pulmonary complications

The blood electrolyte changes in the patients who recovered are those usually observed following surgical trauma of this magnitude elsewhere in the body[30] The depression of the sodium, greatest during the first 2 days after the operation, is a dilutional phenomenon caused by the retention of water and the lysis of cells and fat It has been suggested also that sodium may enter the cells as a result of such tissue acidosis as may exist[31] The rise of potassium is related to cellular damage and hypoxia[36] Sealy and associates[37] and others[7] have demonstrated a transient rise of potassium when hypercapnia is reduced Probably this played a part in the moderate hyperkalemia seen in 16 of the patients shortly after the operation In none of them was found a level over 5 9 mEq /L, which is not sufficiently high to seriously affect the heart

Table V. Summary of Data From Patients Who Died Postoperatively

NUMBER		PREOP.	ANESTHESIA	OPERATION	POSTOPERATIVE PERIOD					
					4-6 HR.	1 DAY	2 DAYS	DAYS PRIOR TO DEATH 2 DAYS	DAYS PRIOR TO DEATH 1 DAY	DAYS PRIOR TO DEATH DAY 0
	Circulatory									
5	Pulse rate	90 ± 12	95 ± 11	122 ± 16	103 ± 12	118 ± 7	110 ± 12	120 ± 8	124 ± 13	128 ± 8
5	Arterial blood pressure	135 ± 8 $\overline{70}$ $\overline{5}$	140 ± 30 $\overline{70}$ $\overline{20}$	108 ± 12 $\overline{60}$ $\overline{6}$	99 ± 5 $\overline{70}$ $\overline{5}$	112 ± 12 $\overline{70}$ $\overline{5}$	110 ± 12 $\overline{70}$ $\overline{6}$	106 ± 15 $\overline{64}$ $\overline{9}$	94 ± 8 $\overline{52}$ $\overline{12}$	85 ± 7 $\overline{48}$ $\overline{20}$
	Ventilation									
2	Tidal volume (L./min.)	0.55 ± .04(5)				0.34 ± .03	0.36 ± .03	0.40 ± .04	0.55 ± .10	
5	Respiratory rate	24 ± 3			30 ± 4	29 ± 2	30 ± 4	32 ± 3	34 ± 6	36 ± 5
2	Vital capacity (L./min.)	2.29 ± 1.0(5)				1.18 ± .41	1.32 ± .34			
	(% Normal)	56%				28%	32%			
	Blood Gas									
4	pCO_2	42 ± 4	51 ± 8	60 ± 10	55 ± 5	53 ± 4	48 ± 4	54 ± 4(3)	64 ± 6(3)	81 ± 15(3)
5	pH	7.41 ± .03	7.36 ± .04	7.29 ± .07	7.29 ± .08	7.34 ± .04	7.36 ± .06	7.32 ± .02(3)	7.26 ± .06	7.21 ± .06(3)
4	% O_2 saturation	92 ± 4	82 ± 6	72 ± 14	86 ± 6	89 ± 4	85 ± 10	83 ± 8(3)	76 ± 8(3)	73 ± 5(2)
	Electrolytes									
4	Sodium (mEq./L.)	139 ± 6	134 ± 5	135 ± 3		135 ± 4	129 ± 4		133 ± 3(3)	
5	Potassium (mEq./L.)	4.3 ± .2	4.6 ± .4	4.8 ± .8	5.0 ± .6	5.1 ± .4	4.8 ± .3		4.9 ± .3(3)	5.5 ± .3(2)
4	Ion. calcium (mg. %)	5.0 ± .5	4.8 ± .6	4.6 ± .6	4.0 ± .3	4.3 ± .3	4.7 ± .5	4.8 ± .2	5.1 ± .3(2)	
5	Lactate (mg. %)	11 ± 4	17 ± 3	20 ± 5	23 ± 5	16 ± 3	14 ± 4			34 ± 4(2)

Note: Figures in parentheses indicate number of determinations if different from the numbers at left.

The depression of ionized calcium in the blood has been reported before[9] and is probably the result of retention of inorganic phosphate and the renal loss of calcium following citrate infusions[45] In no instance was a level below 0 75 mM/L seen This also is above the level known to result in cardiovascular failure

Metabolic acidosis, or better "hypoxic acidosis," took place to some extent in all of the patients during the operation, probably due to inadequate perfusion of part of the vascular bed while cardiac output was decreased This required 2 to 3 days to return to normal levels However, the lactate was seldom more than moderately elevated on the morning after operation This suggests that at this time the majority of the tissues were being maintained with adequate perfusion and reasonably normal oxygen tensions

Three patients who ultimately survived and 5 others who died postoperatively manifested serious cardiovascular depression or failure Examination of the case histories and the data in Table V discloses that this circulatory difficulty was preceded by severe respiratory abnormalities This has been noted before and various explanations offered From the observations here reported, it appears that the common factors resulting from the respiratory inadequacy were a prolonged period of progressively increasing acidosis and a moderate to severe hypoxia

Stead[41] suggests that exhaustion might be responsible for the failure to maintain the blood gasses at normal levels Bjork[3] states that a decrease of ventilated alveoli decreases diffusion surface necessitating greater ventilation and produces unfavorable mechanical factors with decreased lung compliance It is true that the patients in this series were breathing at levels near their respiratory reserve, but 3 of the 4 who died did so after assisted respiration had been started Since all showed hemoglobin oxygen saturation ranges from 68 to 82 per cent while breathing oxygen, it appears that a decrease of the ventilation perfusion ratio[10] had taken place This produced a state of hypoxia and metabolic acidosis for which the remaining lung was unable to compensate by the elimination of CO_2 The arterial carbon dioxide tension was over 65 mm Hg and the pH below 7 30 in all 7 patients Those who died had been moderately acidotic for at least 2 days before death An examination of the blood electrolyte levels during the hypotensive period failed to disclose any abnormalities sufficient to account for the circulatory failure

Intact animals made to breathe high concentrations of CO_2 show serious hypotension only at onset and termination of the hypercapnia[7, 3] That this is true in man is suggested by the observations here cited on the patient whose arterial pCO_2 was 145 mm Hg for at least 90 minutes during his operation As was pointed out, a number of patients were quite acidotic immediately following the operation without serious sequelae, if the pH was normal on the following morning Thus, it appears that short periods of intense respiratory acidosis are not lethal

Nahas and Cavert[39] have pointed out that failure is rapidly induced in the isolated heart by acidosis if circulating epinephrine is not present It might be ued that certain of these patients lacked normal adrenal function. In none the 3 upon whom autopsies were performed was adrenal disease found. Fur- rmore, all of the patients showed a normal tachycardia postoperatively and en exhibited fast pulses until just prior to circulatory failure and death. rge swings of pulse and blood pressure were exhibited on the day before death 3 of the patients. This is similar to the pattern in anoxic dogs observed by owes, Hopkins, and Simeone[7] prior to cardiac arrest. These findings all sug- st that the sympathetic and adrenal systems were functioning in these people.

The fact that the acidosis was prolonged and accompanied by various egrees of hypoxia may be the important matter. Hypoxia of this degree is ompatible with life. Gremels and Starling[20] noted little change in the heart's apability of performing work until oxygen saturation fell to 75 per cent, and ailure did not occur until a critical level of 25 per cent oxygen saturation of he blood was reached.

This situation differs from that encountered in emphysematous patients who are gradually adapted to a combination of hypercapnia and often quite severe hypoxia. Thus, it appears that the presence of acidosis may limit the ability to compensate for even moderate degrees of hypoxia in the relatively acute state.

From a therapeutic standpoint, active measures to prevent or correct prolonged acidosis should be undertaken when possible. The maintenance of normal oxygen tensions may be important in avoiding the serious circulatory consequences of acidosis. Therefore, the administration of oxygen is indicated whenever acidosis is suspected postoperatively except for special circumstances as in patients with emphysema.[38] Finally, arterial punctures and the determination of the pH at times may be of great assistance in the direction of the postoperative care of patients who have undergone thoracic operations.

SUMMARY

1. The cardiovascular response to the trauma of thoracic surgery and to the shifts of blood gas and electrolyte values occasioned by alterations of the respiratory function was studied in 45 patients. The operative procedures included pulmonary resections and others, but none upon the heart. Observations were made before, during, and for a week after the thoracotomy.

2. In general, blood pressure was maintained near normal with only transient depression in the immediate postoperative period. However, during the operation, cardiac output fell 33 per cent on the average, with a decrease of stroke volume. This was accompanied by a rise of total peripheral resistance. Postoperatively this situation was promptly reversed, when the cardiac output rose with a return of normal stroke volume.

3. Although vital capacity and respiratory reserve were depressed to less than one half of those found preoperatively, tidal volume and alveolar ventilation remained near normal except for a few hours after the operation.

4. All of the patients showed moderate postoperative oxygen desaturation of the arterial blood, the least being among those who had been subjected to

pneumonectomy However, the pH and pCO_2 were maintained within the narrow limits considered normal except for the operative period and for a short time thereafter

5 The blood sodium fell on the average to 130 mEq /L on the afternoon *of the operation returning to normal by the third or fourth day* The potassium rose slightly while the ionized calcium level fell 21 per cent to the lowest point several hours postoperatively Concurrently both blood lactate and inorganic phosphate were increased

6 That man can withstand up to 2 hours of severe respiratory acidosis (arterial pCO_2, 145 mm Hg, and pH 6 9) is illustrated by 1 patient who made an uneventful recovery after restoration of normal acid base balance

7 There were 5 patients who died and 3 who were transiently hypotensive but ultimately recovered The course of this group, when compared to those who made uncomplicated recoveries, suggests that in each instance respiratory inadequacy due to atelectasis or pneumonia took place If the resulting hypercapnea (pCO_2 over 65 mm Hg) and acidosis (pH below 7 25) and the moderate accompanying hypoxia were prolonged beyond a few hours, hypotension occurred Circulatory failure and sudden death followed when this situation persisted for 24 hours or more

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DISCUSSION

DR. HERBERT C. MAIER, New York, N. Y.—Dr. Clowes and his associates have indicated the importance of studies which correlate the oxygen, carbon dioxide, and electrolyte alterations with the respiratory and cardiocirculatory changes in the individual patient. By such a means, a better understanding of the early etiologic factors in postoperative complications may be reached.

Too often undue attention is given to one facet without integrating the various chemical alterations that are present, together with the clinical features of that particular patient I think for this reason that Dr. Clowes' studies are of particular value because, as you can see, he has tried to correlate them with the clinical side of the same patient

He referred to the finding that decrease in the arterial oxygen saturation is more likely to occur with a lobectomy than a pneumonectomy This seems to be due to the fact that blood continues to circulate through the remaining lobe on the side where a lobectomy has been performed, in spite of the fact that such a lobe ventilates poorly in the early postoperative period *In other words, you have a discrepancy between the circulation and the ventilation* leading to moderate degrees of hypoxia. That situation does not exist in case of a pneumonectomy.

I should like to emphasize the finding that hypertension during operation was not a frequent finding, in spite of the presence of severe degrees of hypercapnia in some patients As you know, in past years, anesthetists have often considered the development of elevated *blood pressure as a sign of carbon dioxide retention. As is so well known now, there are* no reliable clinical signs of carbon dioxide retention during operation However, in the postoperative period, as has also been shown, hypotension is a common occurrence

Finally, the case that he illustrated, with sudden death occurring on the tenth day, again emphasizes the fact that patients with prolonged moderate hypoxia and carbon dioxide retention may eventually have sudden death occur, so sudden that one thinks of pulmonary embolism and coronary thrombosis, when actually it is just the end result of prolonged chemical disturbance

DR GEORGE W. WRIGHT, Cleveland, Ohio —The papers by Dr Spencer this morning and the one just delivered contain many things that are of interest to the physiologically minded person I hope the authors will forgive me if I do not discuss the particular points raised in their papers, but rather comment on what I think are some very timely implications of these two papers for those of us dealing with thoracic surgery.

The maintenance of body pH within a very narrow range is perhaps the most important requirement for the continuation of life You need not be reminded, I am sure, of the tremendous importance of the respiratory apparatus in providing this constant pH concentration under the daily stresses of life To be sure, the blood has some buffering power and the kidneys over a long period of time are very important for the regulation of pH, but for the hour to hour maintenance of this very essential requirement, the lungs are pre eminent

A patient who comes to us to be treated is commonly impaired in the respiratory apparatus, and then by our very attempts to help him we further impair the respiratory apparatus. In addition, and this is becoming more apparent as we deal with the severely crippled cardiac patient, the proper metabolism in muscle is not going on in individuals who have inadequate blood circulation, and as a result, the stresses in the direction of a metabolic acidosis are commonly greatly enhanced in some of the patients that we deal with We are therefore in the very sticky situation of an apparatus that will not produce the required alveolar hyperventilation to take care of the increased stress in the direction of metabolic acidosis

I think this has been very nicely demonstrated in both Dr. Clowes' and Dr. Spencer's papers Dr. Spencer's paper points out the thing that I think is most important If we wait until there are clinical evidences of this breakdown, we have waited much too long. What we would all like to know is the earliest evidence that the body is getting behind in its ability to compensate and maintain a normal pH The key to the situation is obviously the carbon dioxide tension of the blood.

In so far as I know, there is no clinical sign that will let us know when carbon dioxide sion is beginning to become altered. If we had such a sign, I think that I would not be e making this comment at the moment, because you would then all be aware in plenty of ie to try to do something about your patient and wouldn't be waiting until the end of the blem.

I think it behooves us, therefore, to introduce into our routine care of patients something ıt will give us the evidence that carbon dioxide excretion is not keeping pace with its oduction or with the production of other acid metabolites. There are methods available. han't take the time to go into that. It is true that they are somewhat time consuming and quire some personnel. I would suggest, however, that we introduce into our routine posterative care, and I say "routine" because few of us will do it on any other basis, some easure of the CO_2 tension in the blood in order that we can give these people respiratory sistance long before they are so exhausted as to require some kind of an external pump.

DR. JOHN H. GIBBON, JR., Philadelphia, Pa.—I wish not only to congratulate eorge Clowes on a very nice physiologic study but to ask him whether in any of these inical cases there had been instances in which hypoxia and hypercapnia had not coincided, they did in the patient that died on the tenth day.

About 2 years ago, in *The Journal of Clinical Investigation,* Holaday concluded from udies of patients with mild hypercapnia that respiratory acidosis produced metabolic acidosis. his had not been in accord with all our observations. Last December, we reported before ie Southern Surgical Association experimental studies in which we produced pure hypercapnia ithout hypoxia and pure hypoxia without hypercapnia. We found no evidence that metabolic cidosis, as evidenced by a decline in buffer base and an increase in lactic acid, occurred with ypercapnia, but these changes invariably occurred with hypoxia.

I well realize that metabolic and respiratory acidosis are both present in most patients ostoperatively, as in the case Dr. Clowes presented. However, one condition does not produce he other experimentally. In fact, hypoventilation produces a fall in the blood lactic acid ather than a rise.

DR. CLOWES (Closing).—I think Dr. Maier's and Dr. Wright's points about the ieed for knowledge of the presence of hypercapnia and an understanding of the mechanisms vhich produce it are very pertinent. By way of therapeutic implications, it would appear, and am afraid I didn't have time to go into this, that one should administer oxygen in questions of doubt to convert the patient of a mixed situation, if possible, into the purely acidotic one until something can be done about it. It appears that one can stand hypercapnia better in the presence of arterially saturated blood than otherwise.

I feel that there are two methods available to every surgeon who has access to any kind of laboratory. One is to stick needles into the arteries and simply measure the pH and then find out what the CO_2 combining power is and make an educated guess. If he can arrange to use the bubble technique of Reilly to measure the pCO_2 and oxygen tension, he is in good shape.

Dr. Wright drew to my attention, as we came out here the other day, that rebreathing—not exchanging but rebreathing—into an infrared analyzer will give a pretty good idea of what the CO_2 level in the arterial blood is. The lack of clinical signs of hypercapnia makes it very essential to know about this sort of thing.

Dr. Gibbon, I would agree with you completely on the matter of the difference in lactic acid production in the presence of hypercapnia. About 1955, I think, we presented a paper, also on dogs, distinguishing between hypoxia and hypercapnia, at the American Surgical Association, and our experience in that circumstance was exactly the same as yours. However, in the absence of hypoxia, lactic acid does rise considerably during operations, as many people have pointed out. This, in all probability, is more related to the depression of cardiac output and to the inadequate perfusion given various vascular beds On the other hand, I think that some emphasis should be made of the role of the liver in relation to lactic acid. A poor liver or a depressed one cannot deal with lactic acid as fast as the normal liver, therefore, perhaps the anesthetic, hypercapnia or hypoxia, has something to do with this situation

I would say that we have not seen in the postoperative situation a clinical case that was purely hypercapnic. The average patient is slightly hypoxic, but his pCO_2 is perfectly normal.

PERICARDIECTOMY FOR RELAPSING PERICARDITIS AND CHRONIC CONSTRICTIVE PERICARDITIS

W. S. Blakemore, M.D., H. F. Zinsser, M.D. (by invitation),
C. K. Kirby, M.D., W. B. Whitaker, M.D. (by invitation),
and J. Johnson, M.D., Philadelphia, Pa.

DECORTICATION of the heart is widely accepted as the surgical treatment of chronic constrictive pericarditis. There remains some difference of opinion as to the surgical approach and the extent to which the pericardium must be removed.[1] Early reports of Délorme,[2] who described the pericardiectomy, and the more recent reports of Mannix and Dennis,[3] and Shumacker and Harris,[4] who advocate pericardectomy in patients with chronic effusion and cardiac tamponade, indicate the increasing acceptance of earlier operation. We present for consideration a proposal to remove the diseased pericardium before scar contracts to the extent of reducing the efficiency of the cardiac mechanism. This is not proposed as a treatment for patients with acute pericarditis, but rather for those in whom the relapsing character of the disease has been established even in the absence of cardiac constriction or tamponade. Holman and Willett[5] recommended early surgery in patients with proved tuberculous pericarditis. The 4 patients which they reported had developed severe cardiac impairment prior to surgery, but they clearly recognized the desirability of early surgery and pointed out the ease of dissection when the effusion was present, in contrast to the difficulties encountered when the operation was delayed until the pericardium and myocardium were intimately fused. Antimicrobial therapy now provides considerable protection against dissemination of the disease following operations performed while the tuberculous process is still acute, and the fear of dissemination should no longer unduly delay operation in these patients.

For a number of years, we have performed pericardiectomy and decortication of the heart in patients with pericardial effusion in the absence of proved tuberculosis and prior to the time when they have classical findings of myocardial constriction. Among the many patients who have acute pericarditis, a few have the clinical findings which we believe can be recognized by rather typical symptoms in which the relapsing character of the disease is a prominent feature.

From the Harrison Department of Surgical Research, The Edward B. Robinette Founda- [illegible] Research, The Hospital and School of Medicine of the University of [illegible], Pa.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

All of these patients have had an acute illness, usually easily diagnosed as pericarditis and associated with pleuritis and slight pleural effusion Following symptomatic nonspecific treatment, the patients appeared to make a good recovery when the process was rekindled by physical exertion which was often mild Chest pain, malaise, fever, pericardial friction rub, changes in electrocardiogram leukocytosis, anemia, increase in the sedimentation rate, and reversal of the serum albumin to globulin ratio were commonly found Progressive changes in the cardiac silhouette were noted by roentgenographic examinations (Table I) Repeated hospitalizations were required (Table II) and the patient approached cardiac invalidism accompanied by misery and despair[6 8] The process was quenched by bed rest and medical therapy and, prior to recognizing the typical course of the disease, there was reluctance to recommend surgery for these patients When they returned to their normal activity, the disease was reactivated and the process was repeated with greater irreversible damage The loss of work and livelihood was impressive, and only 20 per cent of the time from the onset of symptoms to the time of operation was utilized in gainful employment by these patients (Table II) Actually, only 2 patients were able to work during any part of the time following the onset of their symptoms and 1 of these continued as a salesman only by his extraordinary persistence, despite his constitutional symptoms

TABLE I CLINICAL FINDINGS

Fever	Electrocardiogram changes
Pain	Leukocytosis
Malaise	Anemia
Weight loss	Increased sedimentation rate
Pericardial rub	Change in cardiac size by x ray
Pleuritis or pneumonitis	

The patients with relapsing pericarditis had an initial acute episode easily diagnosed as pericarditis These symptoms and laboratory findings were commonly found The changes in the cardiac silhouette were not found in 1 patient and evidence of mild constriction was found in only 2 patients In both of these patients operative treatment had been recommended prior to the evidence of constriction

TABLE II PREOPERATIVE HISTORY (8 PATIENTS)

		AVERAGE	TOTAL
Duration of symptoms	1 25 11 5 mo	5 mo	40 mo
Hospital admissions	1 4	3	23
Per cent of time in hospital	20 100	50	(20 mo)
Per cent of time at work	0 40	20	(8 mo)

A prominent feature in the evolution of our recommendation of surgery for relapsing pericarditis was the prolonged invalidism with frequent hospitalization and inability to continue gainful employment from the time of the initial symptoms

Constriction or tamponade in a mild form was noted in only 1 of these 8 patients during a late phase and prior to the time we were recommending early surgical removal of the pericardium which was not overtly interfering with the cardiac function In the earliest period, the operation was infrequently suggested and the suggestion poorly received by physicians Most patients were known to recover from the acute episode of pericarditis regardless of the etiology

Only in the unusual instance when the process of healing contracted the pericardium sufficiently to constrict the heart was surgical treatment accepted prior to the time when the relapsing character of pericarditis was recognized.

In another group of patients, the disease was insidious and the first attack of pericarditis was actually so benign that when constriction had developed, the diagnosis could not be made with certainty.[9] When calcification is present in the pericardium, the diagnosis of constrictive pericarditis is usually considered, but, when calcification is not present and the classical findings of constrictive pericarditis are not found, there is often a reasonable doubt of its presence in a patient with severe myocardial insufficiency. In a number of patients it has been necessary to do an exploratory thoracotomy through a left anterior intercostal incision to determine the presence or absence of pericardial disease.[11] Fortunately, in those patients on whom this procedure has been done, no deaths have occurred except in 1 of our first patients more than 10 years ago. In this patient, the incision was too small and the constrictive pericarditis which he had was unrecognized at the time of operation.

Among those patients in whom the diagnosis of chronic constrictive pericarditis is established, a prominent feature is often ascites. They frequently give a history that for many months or years their treatment has been directed with the diagnosis of ascites or cirrhosis of the liver while they continued as semi-invalids under the care of their internists. In patients with a moderately enlarged heart without pericardial calcification, it may be extremely difficult for the best cardiologists to be certain as to whether or not constrictive pericarditis contributes to the clinical findings. When the patient reaches the surgeon, the healing process has usually advanced and the pericardium is tightly attached to the myocardium. The surgical removal of the pericardium from the myocardium may be tedious and difficult. The patient is often in chronic cardiac failure, may have long-standing liver damage and ascites, and may be a poor surgical risk. Such a patient requires intensive preoperative treatment, a skilled and experienced anesthetist, and meticulous care to assist him through the period of surgical care. Among the 28 patients with chronic constrictive pericarditis whom we have treated, there have been 3 operative deaths. All of these deaths occurred in patients with long-standing heart failure. It would appear better to remove the diseased pericardium early in the course of the disease before the process is advanced, at a time when the patient's heart is not constricted and the patient is a better operative risk. At this time the removal of the pericardium, as well as the complete surgical care, is easier (Table III).

TABLE III. PERICARDITIS—OPERATIVE MORTALITY

	PATIENTS	DEATHS
Pericarditis, chronic constrictive	28	3
Pericarditis, recurrent nonconstrictive	8	0

Among the 25 patients with cardiac decortication for chronic constrictive pericarditis, there were three operative deaths compared with no operative deaths following operation for relapsing pericarditis. In the latter patients the operation is easier and morbidity is appreciably less. This operation is not recommended for acute pericarditis but it is indicated for relief of symptoms and disability incurred with the relapsing form of the disease as well as prophylactic in preventing the development of chronic constrictive pericarditis.

In the preoperative preparation of these patients, diuretics, digitalis, antituberculous therapy, and bed rest are utilized Although the diagnosis of active tuberculosis is not proved, these patients are given antituberculosis therapy during the preoperative and postoperative periods until reports from pathologic and bacteriologic examinations are available to exclude the diagnosis of tuberculous pericarditis Steroid therapy is probably not helpful

The choice of approach in these patients has been individualized and, while wide exposure is desirable, the condition of the patient often does not permit the extension of the procedure that is necessary to obtain such exposure In patients with constrictive disease, a transsternal incision is used[10, 11] In very poor risk patients or when the diagnosis is uncertain, the incision is started as a left anterior thoracotomy incision and, if indicated, is extended across the sternum into the right anterior thorax In the patients with relapsing pericarditis, the midline sternal splitting incision provides adequate exposure[11] The pericardium is resected widely and, whenever it is necessary, the epicardial layer is removed from the ventricles, although it is usually insignificant in extent The operative area is drained via the pleural space The pericardium has not been tightly fused with the myocardium and the operative procedure has proved to be easy In the chronic cases of constrictive pericarditis in which the pericardium is more tightly adherent we use the transverse incision with wide exposure to both pleural cavities in the event that the cardiac cavity might be entered during the dissection Rupture into the ventricle was the cause of death of 1 of our early patients in whom the exposure was inadequate to permit recovery from this catastrophe The dissection should not be extended beyond the area where the exposure permits recovery The thin walled atria are especially vulnerable The pericardium should be removed from phrenic nerve to phrenic nerve, the diaphragmatic surface, and, in most instances, it can also be resected on the left side posterior to the phrenic nerve We have usually freed the pulmonary veins and venae cavae where they enter the pericardium but in no instance has sufficient constriction been found to be certain that obstruction at this point was a major factor in the disease The removal of the constricting tissue over the ventricles appears to be the factor of greatest importance

TABLE IV POSTOPERATIVE HISTORY (8 PATIENTS)

		AVERAGE	TOTAL
Deaths	None		
Hospitalization	12 24 days	16 5 days	131 days
Returned to work	2 2 5 mo	2 1	17 mo
Per cent working	100	100	100

Among these patients who had pericardectomy and cardiac decortication for relapsing pericarditis there have been no deaths hospitalization after operation has been short all the patients have returned to their previous work before 2½ months and none has had a recurrence of his symptoms

Except in those patients with evidence of constrictive disease, we have recommended the operation only to those patients with repeated acute episodes of the disease or to those who have reached the smoldering phase described earlier[7] In no instance to date have any of the patients had recurrence of their pericarditis and, in each, the recovery has been rapid and apparently complete

(Table IV). The presence of pericardial fluid may also be an indication for early operation. We have recently had the opportunity to observe 2 additional patients. Each developed an acute febrile illness with massive pericardial effusion. In each, the large cardiac silhouette rapidly decreased in size and, in a period of 3 and 4 weeks, respectively, frank constrictive pericarditis was present. Although the operative procedure was not technically difficult in either patient the removal of the pericardium may have been easier if the procedure had been carried out earlier.

No specific etiology of the pericarditis has been found in any of the 8 patients with relapsing disease, and in only 4 of the 28 patients with chronic constrictive disease was it proved to be due to tuberculosis. The exact mechanism by which the operation terminates the febrile relapsing illness is not clear. The extensive removal of diseased tissue may eradicate the focus of infection, but this explanation is not entirely satisfactory because of the associated pleuritis and mediastinitis and since the posterior portion of the pericardium is not excised. The removal of diseased tissue accompanied by adequate drainage of the pericardium are undoubtedly additional factors. Button biopsies and windows in the pericardium[12] are less apt to provide adequate drainage and may seal over to give a recrudescense of the disease[8] and we do not consider these procedures adequate. We have not removed large portions of diseased pleura when it is found in patients.

In the postoperative period, overhydration is avoided and the patients are ambulated slowly. With the relief of their symptoms they may feel sufficiently improved to exercise without appropriate regard for the fact that the myocardium is usually involved in the disease process. For this reason they have been given a schedule of limited activity for the first month.

The results after pericardectomy in patients who have had relapsing nonconstrictive disease have been gratifying. All of the patients have returned to their original employment within 2½ months after operation (Table IV).

SUMMARY

1. Patients with constrictive pericarditis have often been permitted to remain in cardiac failure with secondary liver damage and ascites far longer than seems reasonable.

2. Decortication of the heart in the presence of chronic constrictive pericarditis may be difficult because of the technical problems imposed by fusion of the periardium and epicardium and because of the associated dysfunction which accompanies chronic cardiac failure.

3. Pericardectomy and decortication of the heart should be carried out before the patient becomes a poor surgical risk due to the deterioration associated with cardiac constriction and during the time when surgical removal of the pericardium is an easier procedure.

4. The pericardium in patients with tuberculous or idiopathic pericarditis and pericardial effusion should be removed without waiting for the development of constrictive pericarditis.

5. There is a group of patients who have recurrent bouts of nonspecific acute pericarditis who may suffer considerable long-term disability as a result of their disease These patients should have a pericardectomy and cardiac decortication. In 8 patients with relapsing disease of this type, all have had excellent clinical results following operation.

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DISCUSSION

DR JOHN F. HIGGINSON, Santa Barbara, Calif—The notion of trying to prevent the rather horrendous end result which we all have seen in advanced, chronic, long standing constrictive pericarditis is commendable and this should be done, certainly, if we can possibly do it.

However, I was also attracted by what was in the abstract of the essayists' paper regarding difficulties in the diagnosis of some of these cases, despite intensive investigation preoperatively. In order to show one of the surprises that may be encountered at the time of exploration of a patient in whom suggestive findings are present, and who is not left unexplored for many years, I would like to show one slide and describe a patient who had all of the typical findings of congestive failure with all of the angiocardiographic and catheterization studies typical of constrictive pericarditis

This 48 year old woman had had 1 year of dyspnea on exertion with some ankle edema. These symptoms increased and progressed, and she finally developed anasarca with distended neck veins but with a quiet heart which was moderately enlarged and with an unremarkable electrocardiogram except for incomplete right bundle branch block and low voltage. The diagnosis was made clinically of unexplained myocarditis with myocardiofibrosis. She continued to develop more and more edema and then developed ascites When she was first seen by Dr Leonard Rose, of Portland, Oregon, he performed right heart catheterization on Nov. 14, 1957, and obtained the findings of narrow pulse pressure, very high diastolic pressure in the right ventricle but with normal systolic pressure in the right ventricle and pulmonary artery. A marked characteristic dip and plateau were present, and fluoroscopy showed diminished cardiac pulsations.

I explored this patient on Dec. 3, 1957, and here [slide] you can see the enlarged heart that was encountered. The pericardium was perfectly normal. However, a very remarkable finding could be easily noted as one watched the heart. The ventricles came to a sudden, sharp, slapping termination of diastolic filling about halfway of what one would expect, quite obviously suggesting stiffening of the myocardium. A biopsy of the right ventricular myocardium was done with a Silverman needle, and a biopsy of the right auricular appendage was taken in the usual manner. The appendage and the right atrium were greatly dilated and enlarged.

Pathologic examination established a diagnosis of primary amyloidosis. Cardiac mural disease, therefore, is another explanation that must be taken into consideration whenever the clinical picture suggestive of constrictive pericarditis is present, despite highly suggestive findings by angiography and catheterization studies.

DR. SAFUH ATTAR, Baltimore, Md.—I would like to ask Dr. Blakemore three questions.

The first one is, what is the earliest time interval elapsing between the onset of the disease and the pericardiectomy among the 8 patients operated upon?

Second, will you operate on a patient with a clinical picture of pericarditis with a venous pressure of 300 which, on medical treatment, came down to normal, but clinically the patient persisted in having evidence of recurrent acute pericarditis, as done in your cases?

The third question is, in case the patient definitely has recurrent acute pericarditis, as shown in your cases, and does suffer of myocarditis, would you interfere early or would you wait until it goes to the chronic stage and then interfere?

DR. J. GORDON SCANNELL, Boston, Mass.—I should like to say how much I have enjoyed this presentation and to emphasize a point which was mentioned; namely, the importance of doing a liberal decortication of the ventricle at the time of the initial procedure.

We have had the opportunity to see a few late recurrences among the very early cases of Dr. Churchill, and also recurrences in 1 or 2 patients operated upon during a relatively acute phase and a radical decortication not done. In these recurrent cases, the source of the difficulty has invariably been on the posterior aspect of the left ventricle, in the region of the junction between the left atrium, the left pulmonary veins and the atrioventricular groove. Had we always been insistent on getting away back to this point at the original operation, when it is relatively easy to do through a left anterolateral approach, especially in a subacute phase of the disease, I am quite certain that this recurrence could have been avoided.

Constrictive pericarditis, as you know, seems to be a disease primarily of the pericardium itself, not the pericardial cavity, and it is important to resect the pericardial sac, not merely just free up the heart.

DR. EDGAR P. MANNIX, Manhasset, Long Island, N. Y.—I think Dr. Blakemore is to be congratulated for his excellent presentation in drawing our attention to not only the very important clinical entity of chronic constrictive pericarditis, but also, what is more important, I believe (because it is less well understood), the place for the surgical treatment of chronic pericarditis during the stage of effusion.

Patients with the latter type of problem are most difficult to acquire. In my experience, internists are reluctant to advocate surgical treatment for patients suffering with chronic pericarditis with effusion, yet, I am sure, as Dr. Blakemore will agree, that the operation is much easier to do during the stage of effusion and the deleterious effects of chronic constriction can be avoided.

This point, of course, has been made many times in the past. Dr Emile Holman more than 5 years ago, as a matter of fact, advocated pericardiectomy during the acute phase of tuberculous pericarditis. Dr. Barker, among others, from the University of Michigan, has reported a case of chronic pericarditis with effusion which lasted for as long as 6 years and then went on to constriction

I would like to close my comments by simply pointing out that in keeping with Dr Higginson's comments, the diagnosis is very important We believe it is important to exclude pericarditis with effusion when it is on a rheumatic basis, because this almost always means active rheumatic carditis In our opinion these people should not be operated upon at that time

There is another entity that occurs in small children and infants which is very difficult to diagnose, sometimes accompanied by pericardial effusion, namely, the idiopathic chronic myocarditis. There are other medical entities, myxedema with pericardial effusion for example, is one which can confuse the diagnostic picture and which can be treated medically by thyroid medication

DR EMILE HOLMAN, San Francisco, Calif —This presentation has pleased me very much as it recognizes the need of a radical pericardectomy when operating for constrictive lesions.

I would like to place on record a patient who had been operated upon three times for constrictive pericarditis, and who still had his ascites He remained in a Marine hospital for over a year, having his abdomen tapped periodically for recurring ascites

We operated upon him again with great reluctance, and in the course of the operation we accidentally entered the right ventricle, and had considerable difficulty extricating ourselves from that situation Because of the patient's poor condition, I was unable to remove any pericardium I did, however, incise the pericardium directly over the inferior vena cava, spreading the edges of the thickened pericardium for about 2 cm , and did the same over the superior vena cava

This patient has not required tapping since that operation, indicating the great importance of liberating all critical areas, in this case the inferior and superior venae cavae which had escaped adequate liberation at the three previous operations

DR BLAKEMORE (Closing) —I believe the questions can be divided into two groups corresponding to the separation we have made in the presentation This may avoid confusion, since we have discussed a form of pericarditis which we have called relapsing pericarditis and also discussed many of the difficulties which have occurred in the diagnosis and treatment of chronic constrictive pericarditis

Dr. Higginson's comments again emphasize the difficulties of establishing the diagnosis in patients with chronic constrictive pericarditis We have found that excellent cardiologists with the benefit of modern diagnostic techniques have been unable to eliminate the diagnosis of constrictive pericarditis in patients who are severely ill and have congestive heart failure of unknown etiology. In these instances, an exploratory *operation is often necessary diagnostic procedure The earliest time that we have been* able to definitely recognize the signs and symptoms of relapsing pericarditis has been 6 weeks, and we were able to do this only in 1 of the latest patients whom we have seen The principal point in making the diagnosis of relapsing pericarditis is to recognize the smouldering phase in a patient in whom the disease can be rekindled by physical activity, can be quenched by bed rest and medical therapy, and reactivated as physical activity is *again increased* Dr. Harry Zinsser, a medical cardiologist in our group, has been speaking to groups of internists, and as this type of disease is better recognized the surgeons will see many of these patients earlier in the course of disease

Dr. Attar asked a question about a specific patient who had increased venous pressure and recurrent episodes of pericarditis I believe this is a patient in whom we would recommend removal of the pericardium If we could recognize the relapsing form of the disease early in its course, we would recommend an early operative procedure However, the operation is not to be recommended for every patient with acute pericarditis. Chronic constrictive pericarditis may in contrast follow an unrecognized episode of acute pericarditis, and an earlier operation would be desirable for these patients prior to the onset of the severe myocardial changes which accompany long-standing constriction.

We are honored to have Dr. Holman discuss this paper since his earlier publications have strengthened our position in advocating early operative procedures for our patients. With regard to the patients which Dr. Holman mentioned, we are in agreement that no operative procedures are indicated for the treatment of pericarditis of rheumatic origin, but pericardiectomy is indicated for the patients with idiopathic relapsing or tuberculous pericarditis. In these patients, early operation is desirable before extensive myocardial damage occurs which significantly increases the operative risk. Dr. Holman and Dr. Scannell advocate extensive resection of the pericardium, and we are again in agreement. We make some reservation and present that, in certain patients who are severely ill and in whom the operation of this magnitude increases the operative risk, the procedure can be shortened. The diseased pericardium about the atria and veins is left, but the pericardial and epicardial layers are removed from the ventricles.

Délorme, who utilized the cardiolysis procedure and described the principles of the pericardiectomy operation, was critical because the operation did not remove the epicardial layer. Many patients require the removal of this layer as well as the pericardium, but the epicardial layer has not been of significant thickness in some patients whom we have treated with relapsing pericarditis to warrant removal.

THE RESULTS OF SURGICAL CORRECTION OF ATRIAL SEPTAL DEFECT COMPLICATED BY PULMONARY HYPERTENSION

Harold V. Liddle, M.D. (by invitation), B. W. Meyer, M.D., and
John C. Jones, M.D., Los Angeles, Calif.

ATRIAL SEPTAL DEFECT of the secundum type is the most successfully managed intracardiac defect to which surgical attention has been turned. In the last 10 years, a variety of surgical techniques has been devised for its closure. In 1948, Murray[1] described obliteration of the defect with fascia lata strips. Later, Gross,[2] Bailey,[3] and Sondergaard[4] described blind operative procedures which have been very successfully applied.

Presently, open heart methods make possible direct accurate suture of the anomaly with low mortality. The majority of patients with secundum atrial septal defects have normal or minimally elevated right ventricular and pulmonary artery pressures. This defect, unlike ventricular septal defect, is almost never complicated by pulmonary hypertension in children. Approximately 15 per cent of these patients in adolescence and adulthood do have pulmonary vascular obstruction. Repair of the defect in the presence of severe pulmonary vascular obstruction increases the morbidity and mortality tenfold.

PHYSIOLOGY OF ATRIAL SEPTAL DEFECT

The physiologic characteristics of secundum atrial septal defects are unique. At birth there is little flow across the atrial defect, but as systemic resistance increases a left to right shunt develops. The volume of this shunt gradually becomes larger and results in pulmonary flow which may be two to three times systemic flow. To accommodate this volume of blood, the pulmonary vessels dilate and their resistance falls. The right ventricle becomes overloaded by this increasing burden, particularly during the diastolic phase. It dilates in response to the demand, and the electrocardiogram reflects this dilatation as delayed conduction. Prolonged exposure to excessive flow is occasionally associated with morphologic changes in the pulmonary vessels resulting in pulmonary hypertension. In the presence of severe pulmonary vascular obstruction, the volume of shunt is reduced but remains predominantly left to right.[5, 6]

From the Department of Surgery, University of Southern California Medical School, Los Angeles, Calif.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

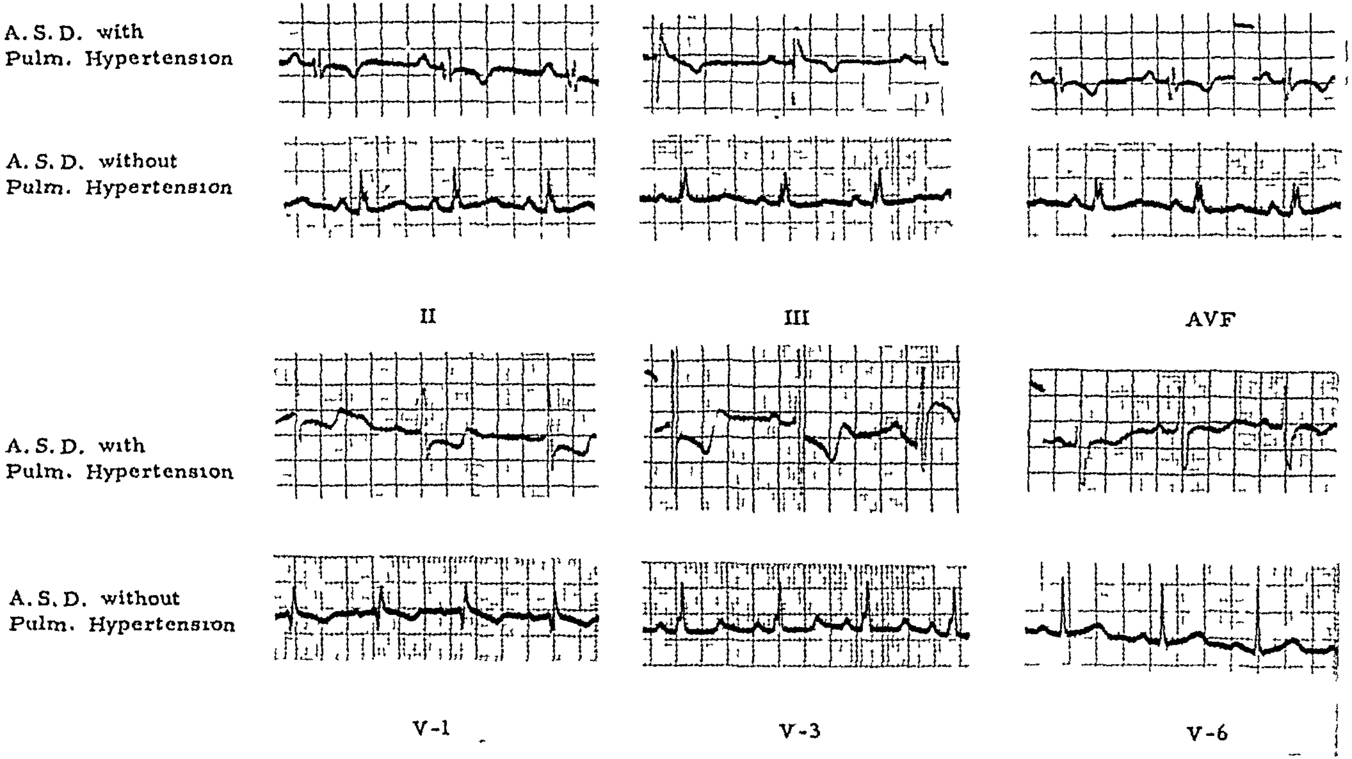


Fig. 1 —Electrocardiogram in atrial septal defect, with and without pulmonary hypertension.

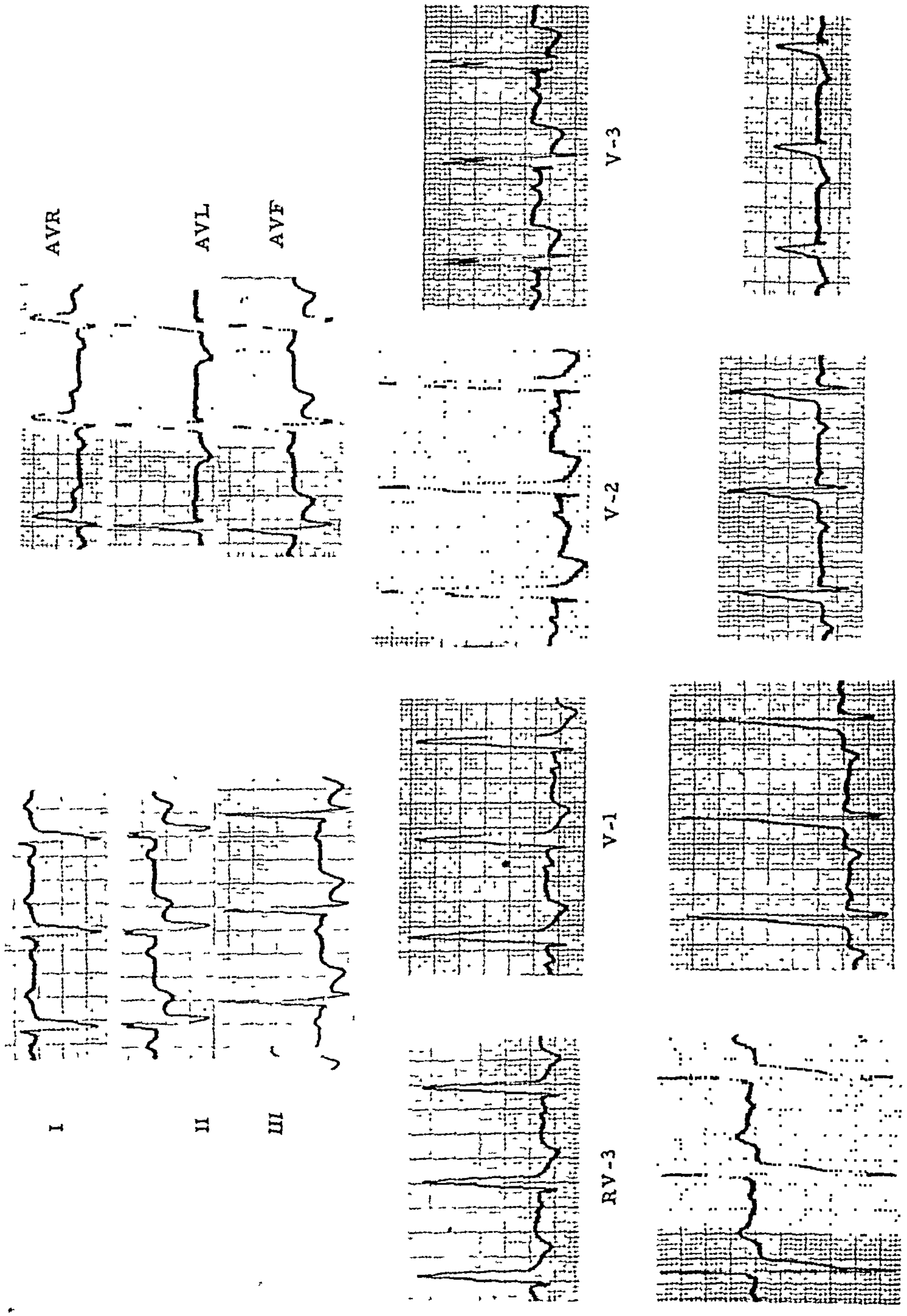


Fig. 2.—Electrocardiogram in atrial septal defect with severe pulmonary hypertension.

Even with a reduction of shunt, right heart work actually increases as pulmonary resistance increases Closure of an atrial septal defect, complicated by severe pulmonary vascular resistance, is often associated with acute right ventricular dilatation, fibrillation, and death Selection of patients with severe pulmonary hypertension who will tolerate closure of the defect is difficult, and evaluation of pulmonary artery pressure alone is not a sufficient criterion

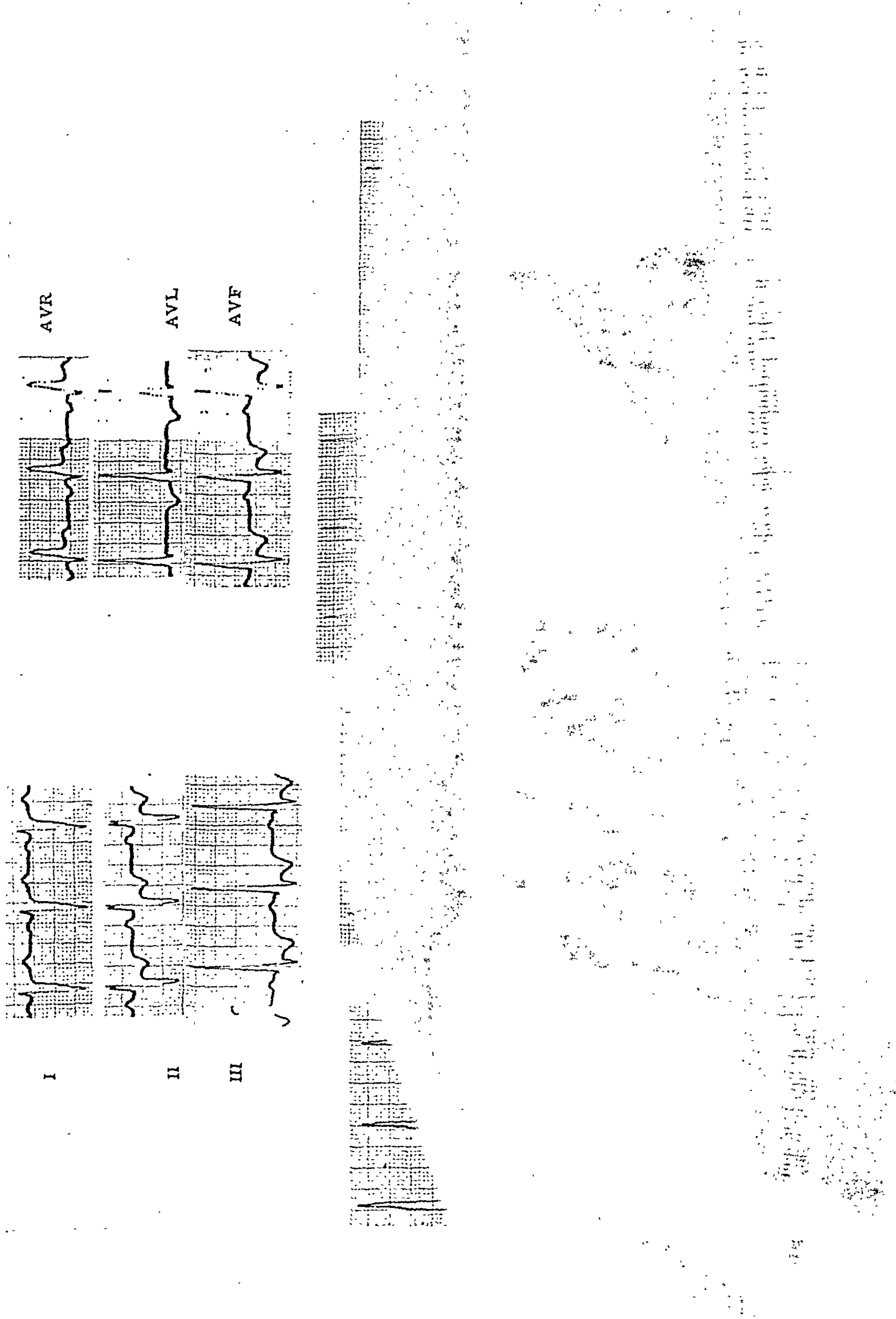
REPORT OF CASES

During the last 5 years, over 180 patients with atrial septal defect of the secundum type have been surgically treated in our unit One hundred forty of these patients, who had normal pulmonary artery pressures, were operated upon without mortality We consider pulmonary artery pressures in excess of 50 mm Hg to constitute pulmonary hypertension The 15 patients in this series with simple secundum atrial defects, complicated by pulmonary hypertension form the basis of this report Their ages ranged from 16 to 56 years, an average of 39 years There were 11 women and 4 men

Symptoms—These patients all exhibited progressive dyspnea and fatigue Two had recurrent hemoptysis Four patients developed chronic atrial fibrillation, and 2 had been in congestive failure Half the patients suffered chest pain Cyanosis at rest was present in 4 patients One patient had previously undergone exploration with a mistaken clinical diagnosis of mitral stenosis The 16 year old girl had very advanced kyphoscoliosis and pulmonary fibrosis The progression of symptoms in these patients was characteristically rapid, an important event in evaluating the risk in these patients Cardiac physical findings revealed cardiomegaly and right ventricular heave in all but 2 patients There was a loud systolic murmur heard along the left sternal border in the third to the fifth left intercostal spaces Seven patients had a blowing diastolic murmur in the third to fourth left intercostal spaces The second heart sound was, in each case, markedly accentuated and widely split

X ray Findings—Preoperative x ray studies of the chest of each patient were reviewed, and the cardiac silhouette was of normal size in 2 Cardiomegaly in the remaining patients varied from slight to severe The main pulmonary artery shadow was enlarged in all cases—strikingly so in 4 Hilar vessels were enlarged in every case The relative sizes of peripheral and hilar vessels were then compared Instead of the peripheral engorgement usually associated with atrial septal defect, these patients exhibited disproportionate diminution in the caliber of peripheral vessels when compared to the hilar vessels In the x ray studies of patients who died at operation, heart size was not particularly increased, but the pulmonary artery segment was exceedingly large The discrepancy between peripheral and hilar vessel size was most marked in these individuals Cardiac size could only occasionally be correlated with the degree of pulmonary hypertension

Electrocardiographic Findings—Electrocardiograms revealed right ventricular hypertrophy in all but two instances (Fig 1) One of these 2 patients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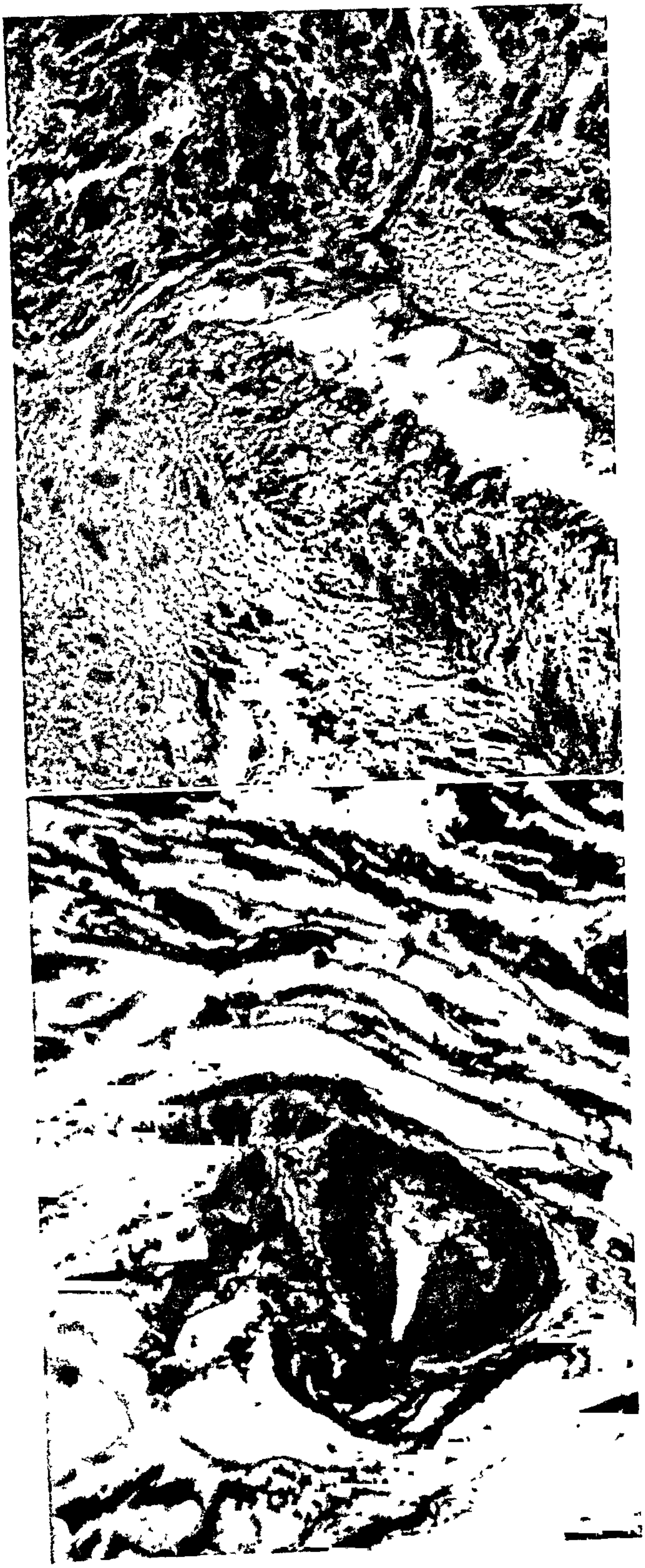

Fig. 3.—*A*, A subpleural small artery, with medial hypertrophy, shown emptying into a glomeruloid structure. *B*, High-power detail of the same vessel showing the glomeruloid structure and vascular lake emanating from it.

were seen occasionally to follow alveolar septa, but more often to drain directly into veins. There is divided opinion in the literature[10-13] about the function of these structures. We are inclined to feel that they may be arteriovenous shunts because they were seen in a patient who was proved at autopsy to have a healed septum, yet he had been deeply cyanotic for 3 years after surgery.

Eight patients comprise the second group. These individuals tolerated closure of their defects satisfactorily. One died 8 hours postoperatively of hemorrhage from an unrecognized bleeding internal mammary artery. A second patient who survived, has had a re-opening of the atrial septal defect and pulmonary hypertension has progressed. This defect had been closed by the Sondergaard method. The 6 remaining patients have progressed very well with minimal or no limitation of their activity. Five have been followed closely at our institution, and in each there has been decrease of cardiac size, of hilar shadows, and of the second pulmonary heart sound. The sixth patient is reported by her family physician to have comparable improvement.

Four of these patients have been recatheterized from 1 to 3 years postoperatively (Table II). Each has had significant decrease in pulmonary artery pressure. In 1 of these, the right ventricular and pulmonary artery pressures fell from 100 to 50 mm Hg (Table III), and the electrocardiogram showed reduction of right ventricular hypertrophy (Fig 4). The pulmonary artery pressure in a second patient fell from 57/21 to 18/4, and the electrocardiogram showed only minimal evidence of right ventricular hypertrophy. This patient still has respiratory limitation due to kyphoscoliosis.

TABLE II POSTOPERATIVE CATHETERIZATION DATA*

PATIENT	AGE	SEX	SUP V C	P A	R V	R A	B A	FLOW	RESULT
D M	31	M	*70*	15/9 *64*	81/9 *63*	77/35 *59*	93/62 *86*		Dead 3 yr PO in heart failure
P L	41	M	*69*	5/1 *70*	73/0 *72*	73/27 *72*	128/67 *89*		Good—4 yr PO
D B	33	M	9/7 *77*	9/7 *75*	93/8 *75*	93/88 *75*	110/70 *75*		Progressive deterioration —3 yr PO
R B	37	F	10/5 *76*	10/5 *77*	55/10 *77*	55/30 *77*	138/80 *95*		Excellent—2 yr PO
M L	39	F	*66*	6/0 *69*	45/0 *67*	44/18 *66*	128/60 *90*	*3 7* P A *3 4* systemic	Fair—2 yr PO
J C	16	F	*65*	2/2 *68*	18/0 *67*	18/4 *68*	108/60 *94*		Excellent—4 yr PO kyphoscoliosis severe
J B	23	F	9/3 *64*	9/4 *69 83*	70/7 *73 85*	75/25 *75*	103/67 *88*		Recurrence of defect

*Pressures and oxygen saturation (the latter in italics)

In another patient, pulmonary artery pressure, 16 months after operation had only fallen from 100 to 70 mm Hg. Now, 4½ years after operation, pulmonary artery pressure remains high. There is no evidence that the defect has re-opened, but the patient remains cyanotic with exercise possibly due to intrapulmonary shunting. Subjectively, he remains well after return to normal activity.

TABLE III. CATHETERIZATION DATA (R. B., 37, F)*

	SUP. V.C.	R.A.	R.V.	P.A.	B.A.	WEDGE	FLOW
Preoperative data	7/2 *60*	14/6 *71*	100/0 *74*	100/50 *76*	140/90 *87*	10/3	P.A. 2 × systemic by RISA
Postoperative data	10/5 *76*	10/5 *77*	55/10-0 *77*	55/30 *77*	138/80 *95*		

*Pressures and oxygen saturation (the latter in italics).

The electrocardiogram in a fifth patient, who would not be recatheterized, shows disappearance altogether of evidence of right ventricular hypertrophy, and symptomatically she is completely normal.

In summary, of the 15 patients with severe pulmonary hypertension who underwent closure of the defect, 5 died at operation. Two patients were unimproved, and 1 died of an operative complication. Six patients have had long-term survival and show regression of pulmonary vascular resistance. There has been recurrence of the defect in 1 patient.

DISCUSSION

Atrial septal defects are uncommonly complicated by advanced changes in the lesser circulation. Even among adults, pulmonary vascular obstruction is only occasionally present. This indicates that flow alone is not responsible for its appearance.

The size of the defect does appear to be related to the appearance of pulmonary hypertension. In this series, the defects varied in size from 3 to 7 cm., the average being 5 cm. We have had no patients with small defects who have had pulmonary hypertension.

The extreme increase in mortality associated with pulmonary vascular obstruction makes selection of patients for surgery with this complication critical. In this series, mortality was increased from zero in uncomplicated cases to nearly 50 per cent in those with severe pulmonary vascular obstruction. However, the fact that some of these poor risk patients can be permanently rehabilitated compels us to find some means of selection. Cyanosis is an indication of excessive right atrial pressure, and suggests irreversible pulmonary changes. Three of the 4 cyanotic patients in this series either died or were not improved by surgical intervention. A history of congestive heart failure predicted an unfavorable outcome. The degree of pulmonary hypertension in this study was, however, unrelated to the surgical result. Two of 5 patients who died at operation had pulmonary artery pressures below 65 mm. Hg, yet 3 patients who have done well had pressures between 93 and 105 mm. Hg. Neither the duration of symptoms nor cardiac size were related to survival.

Although no single or combination of data are incontrovertible evidence for selection of probable survivors, review of this series does suggest four factors which may be helpful guides. The first two, as mentioned above, are cyanosis and a history of cardiac failure. Patients with this combination will probably not survive operation.

An additional factor is a marked discrepancy between the caliber of hilar and peripheral vessels in x-ray studies In this series the combination of huge hilar vessels and peripheral starving was usually associated with irreversible vascular change Although the peripheral vascular shadows were decreased in all these patients, there was not an unusual discrepancy in vessel size among the individuals with good results

The electrocardiograms of 13 of these 15 patients showed right ventricular hypertrophy Six of the 7 patients with irreversible pulmonary vascular change had severe right ventricular hypertrophy In each case, the secondary R wave in V_3R and V_1, and the S wave in V_6 were strikingly increased With the exception of the 1 patient who had advanced kyphoscoliosis, this magnitude of electrocardiographic change was not seen in the survivors

SUMMARY

Simple atrial septal defects of the secundum type have been surgically treated in more than 180 patients in our unit Of this number, there are 15 patients, all adult, whose defects were complicated by pulmonary artery pressures in excess of 50 mm Hg Five of these patients succumbed at operation and 2 were not benefited by closure of the defect A review of the charts of these 15 patients suggests four clinical and laboratory observations which are related to the surgical failure in 7 patients They are the presence of cyanosis, the history of congestive heart failure, severe right ventricular hypertrophy, and a marked discrepancy in vessel size in chest x-ray studies When two or more of these observations are made in a patient, there probably exist irreversible pulmonary vascular changes

There is evidence that acetylcholine injected in the pulmonary artery may delineate its capacity for dilation Theoretically, acetylcholine and cineangiography in combination may vastly improve our evaluation of the pulmonary vascular bed

The very serious risk and relatively poor results of surgery in this group of patients, compared to the uncomplicated atrial defect, are urgent evidence that these defects should be closed when they are recognized There is nothing to be gained by procrastinating and none of these people will improve with time

We wish to express our appreciation to Donald C Tyler, M D , Assistant Professor of Pediatrics, University of Southern California Medical School and Director of Cardiology Diagnostic Laboratory of the Childrens Hospital Society of Los Angeles and to H G Peterson, M D , Assistant Clinical Professor of Radiology, University of Southern California Medical School and Chief Radiologist of the Childrens Hospital Society of Los Angeles for their help in assimilation of the data presented

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17. Discussion of Watkins and Gross.[15]

Discussion

DR. ALFRED GOLDMAN, Beverly Hills, Calif.—The authors should be congratulated on this paper. I am wondering whether or not in the treatment of pulmonary hypertension with atrial septal defect they have considered or would care to discuss the problem of using a patch with perforations in it, and whether or not they would feel that this might obviate the sudden strain on the right ventricle.

DR. MEYER (Closing).—We have not used a perforated patch to reduce the size of the defect for we have felt that partial closure does not reduce pulmonary hypertension. This belief is based on catheterization data following partial closure of high pressure ductus and interatrial defects with very high pressures. We believe that if there is any release or reversibility of the pulmonary vascular obstruction, it can be determined at the operating table by the way the right heart reacts after defect closure. Invariably, with a fixed resistance in the lungs, the right heart will dilate and fibrillate after the defect is closed. In these patients, the defect had to be re-opened before normal cardiac function could be restored.

COARCTATION OF THE AORTA IN INFANTS

A Clinical and Experimental Study

Thomas H. Burford, M.D., Thomas B. Ferguson, M.D., David Goldring, M.D. (by invitation), and M. Remsen Behrer, M.D. (by invitation), St. Louis, Mo.

THE CUMULATIVE experience in the surgical management of coarctation of the aorta now spans a period of 15 years. It is well established that surgical removal of the constriction with restoration of continuity is the treatment of choice. In older children and young adults, operation can be done at very low risk, with every assurance of cure. Coarctation in infancy, on the other hand, is a less well understood entity and a number of formidable problems and confusing issues still exist. With the development of the flush technique for simple and accurate determination of blood pressure in newborn infants, it has become apparent that the lesion is by no means as rare as once thought, and, indeed, when found in combination with patency of the ductus arteriosus, is one of the leading causes of cardiac failure in early infancy.[1] As more cases are documented, it has been realized that anatomic classifications of coarctation which stress infantile versus adult forms are no longer tenable, for the adult form can cause trouble at 2 weeks of age and the infantile form conversely can go undiagnosed until adulthood. A division on the basis of segment length into long and short segment types is also not too helpful, for one type merges imperceptibly into the other. A more useful classification simply states the relationship of the coarctation to the ductus (preductal, juxtaductal, or postductal) and whether the ductus is open or closed.[2] The association of coarctation in infancy with other cardiovascular malformations, particularly patent ductus arteriosus and ventricular septal defects, is well known, but the importance of patent ductus as a cause of difficulty has not been sufficiently stressed. There are differences of opinion among pediatric cardiologists as to the best method of management of these cases. Nadas[3] feels that a number can be brought out of cardiac failure and carried along until they are several years of age. Calodney and Carson,[4] and Goldring and his associates[5] have stressed the uniformly poor results they have had with medical management, and this led them to urge early surgical intervention. In spite of the prevalence of this lesion in the infant age range, there are relatively few reports of successful surgical treatment. Isolated cases have appeared[6, 7] and the papers of Mustard[8] and Smeloff[9] and their colleagues have included a small group of operated cases. A greater degree of success

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should be possible as more information is gathered concerning the basic as well as the clinical aspects of the disease. This report is an analysis of the total surgical experience at the St. Louis Children's Hospital with coarctation in infants (24 months of age and younger), together with experimental investigations concerning the physiologic derangements associated with coarctation and patent ductus arteriosus.

CLINICAL MATERIAL

Clinical experience with these seriously ill infants since 1940 now totals about 60 proved cases, and only 2 patients have survived beyond infancy on medical therapy alone. This prompted the policy of advocating early surgical intervention. The first operative repair was undertaken in March, 1949 (T. H. B.). Since that time, 16 infants under the age of 24 months have been operated upon. (By comparison, during the same 10-year period, 72 patients over the age of 2 years have been repaired.) There were 11 males and 5 females. The ages on admittance ranged from 9 days to 24 months, but the majority of patients developed difficulty soon after birth. Thirteen of the 16 cases were under 4 months of age. The median age at the time of operation was 6 weeks. Symptoms and signs which brought the infant to the hospital were almost all related to cardiac failure, and as such were not helpful in making a specific diagnosis (Fig. 1). Most frequent were problems of feeding, dyspnea, and tachypnea. Physical examination revealed the signs of overt cardiac failure in all cases, with pulmonary congestion, hepatomegaly (1 to 5 fingerbreadths), and edema (Fig. 2). Five infants had cyanosis which cleared under treatment, and therefore was thought related to circulatory failure. Differential "girdle" cyanosis, supposedly typical of this condition, was not seen. All of the babies had a systolic murmur, graded 4 plus in 4, barely audible in 4, with intermediate gradations in the remainder. None

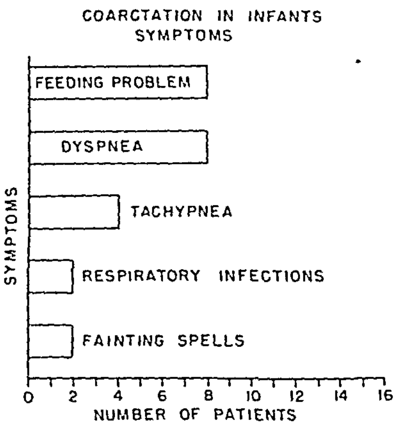


Fig. 1.

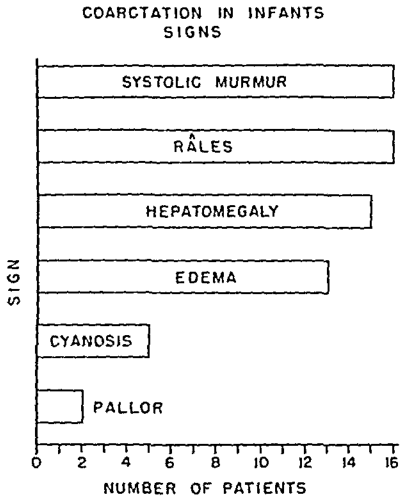


Fig. 2.

Fig. 1.—Symptoms encountered in the 16 infants in this series.
Fig. 2.—Physical signs present in the 16 cases.

had a continuous murmur. Roentgenographic examination of the chest uniformly showed the same picture—a markedly enlarged heart with pulmonary vascular congestion and engorgement compatible with a left-to right shunt and congestive cardiac failure (Fig 3). The electrocardiograms were grossly abnormal. Right ventricular enlargement was present in 9 cases, left ventricular enlargement in 7 cases. A mixed group of 9 children also had myocardial disease. None of the patients had cardiac catheterization, and in only 1 infant was an intravenous angiogram done This policy was dictated by the critical state of these infants, since it was felt that they would not withstand anesthesia for a diagnostic procedure

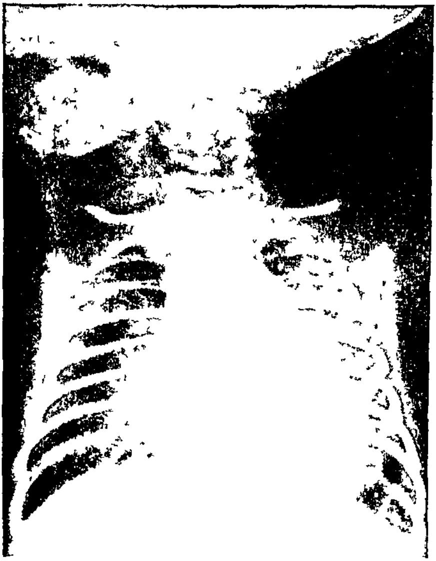


Fig 3—Roentgenogram of an infant with coarctation and patent ductus proved at autopsy There were no other anomalies The enlargement and configuration are typical of all the cases in this series

The single most important examination was the determination of the blood pressure. The flush technique, utilizing the principle of reactive hyperemia, was first conceived and used in 1950, and the method standardized by 1952[10] (Fig. 4). Since that time it has become a routine part of the workup, and several of the infants included here were quickly diagnosed, having been admitted as feeding problems, etc. When the pressures are thought to be abnormal, a number of determinations are made by each of several observers over several days, and the results averaged To be significant, the gradient must exceed 20 mm. Hg. In recent cases, flush pressures have been corroborated by an electronic pulse recorder (Infraton). In all the infants except the first 2, the diagnosis was made by the flush technique. Fig. 5 shows the spread and the average values obtained. A mean gradient of 86 mm. Hg is indicative of the severe degree of coarctation present in these infants.

The average time lapse from admission to operation was 2½ weeks. All the babies showed a temporary favorable response to digitalis. Prior experience had taught that this improvement should not raise false hopes about medical management, for too many infants will improve, then deteriorate rapidly and die. Recently it has been the policy to operate as soon as it is established that serious cardiac failure exists on the basis of coarctation, and the child can be brought into optimum condition.

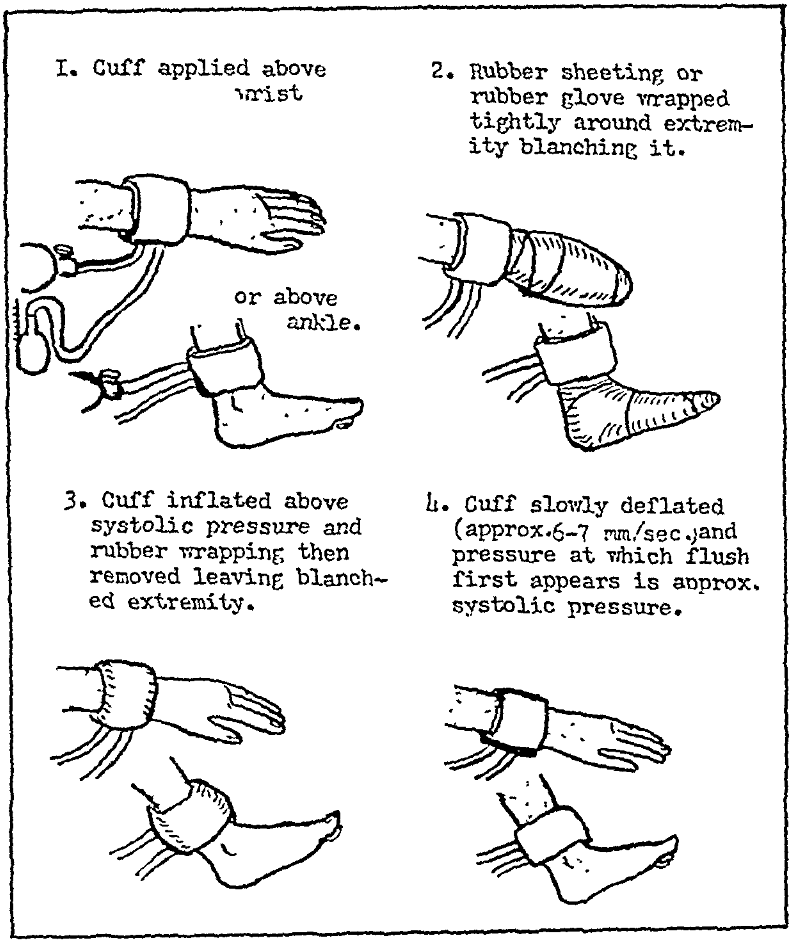

I. Cuff applied above wrist
or above ankle.
2. Rubber sheeting or rubber glove wrapped tightly around extremity blanching it.
3. Cuff inflated above systolic pressure and rubber wrapping then removed leaving blanched extremity.
4. Cuff slowly deflated (approx.6-7 mm/sec.)and pressure at which flush first appears is approx. systolic pressure.

Fig. 1.—Diagram of the flush technique for measuring blood pressure in infants (From Goldring and Wohltmann, J. Pediat. 40: 285, 1952)

Operative Findings and Results.—In all 16 infants the coarctation was complicated by patency of the ductus arteriosus. In 10, the narrow segment was located proximal to the ductus (preductal) and in 6 immediately adjacent to the ductus (juxtaductal) (Table I). It was not possible to classify any case as definitely postductal. There was considerable variation in the length of the narrowed segment, the extremes ranging from a short pinched constriction (4 infants) to involvement of the entire transverse arch (2 infants).

In general, the longer coarctations were preductal in position, the shorter segment varieties juxtaductal The diameter of the ductus was also quite variable, and large and small caliber communications were found in both groups Three infants in Group 1 had shunts equal in size to the aorta

TABLE I COARCTATION IN INFANTS—OPERATIVE FINDINGS
PATENT DUCTUS ARTERIOSUS—16 CASES

	GROUP 1		GROUP 2	
Position	Preductal	10 cases	Juxtaductal	6 cases
Procedure	End to end	4	End to end	6
	Homograft	1		
	Shunt	1		
	None	4		
Survivors		3		6
Deaths		7		0

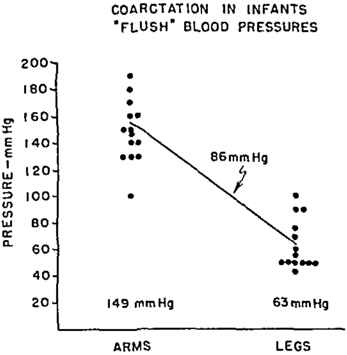


Fig 5—This figure shows the blood pressures obtained by the flush technique in 14 of the infants The gradient across the coarcted segment averaged 86 mm Hg

Mobilization and end to end reconstruction was possible in 4 cases in Group 1, and in all 6 cases in Group 2 The anastomoses were done with running fine silk sutures, interrupted at frequent intervals The first child in the series had involvement of the transverse arch, and the defect was bridged by a fresh homograft The fifth case also involved the arch, and it was felt at the time that a graft could not be properly placed, so the proximal ends of the divided left carotid and the left subclavian arteries were anastomosed Four infants died during thoracotomy before any definitive procedure could be done

There were 9 survivors and 7 operative deaths, a mortality rate of 44 per cent (By comparison, there were 5 deaths in the 72 operated cases over 2 years of age, a mortality rate of 7 per cent, 2 of these were homograft failures) All 7 deaths were in Group 1 patients and occurred either before, during or at the end of operation Cause of death was cardiac arrest in 6 ventricular fibrillation in 1 The mortality rate has declined as experience with these sick children has increased All 5 infants operated upon during the first 5 years died. During the last 5 years there have been 11 cases with only 2 deaths, a mortality rate of 18 per cent for this abbreviated group. These fatalities were in 2 of 4 cases done with hypothermia. Body cooling has not been used since 1956, and there have been no spinal cord sequelae, in spite of rather extensive mobilization of the aorta in several instances.

Follow-Up.—Of the 9 operative survivors, 8 are living and clinically well. One infant, repaired at 3 weeks of age, did better for about 3 months, and then returned with recurrent failure, and signs indicating a severe intracardiac abnormality. It was hoped that he could be improved to the point where open heart surgery would be feasible, but death occurred at 9 months of age. Autopsy revealed a large atrial septal defect of the ostium primum type, with gross deformity of both the mitral and tricuspid valves. The aortic repair was intact, and the diameter measured 12 mm. at the suture line, 17 mm. above and below.

The remaining 8 children have been followed from 9 months to 5 years since operation (average 2 years) (Table II). All are asymptomatic at the present time, although clinically 3 children definitely have an intracardiac left-to-right shunt, and 2 others are suspected of having a small shunt. The remaining 3 do not have additional lesions. Growth and development have followed the normal pattern in all but 1, a child with probable ventricular septal defect, who is exhibiting growth failure.

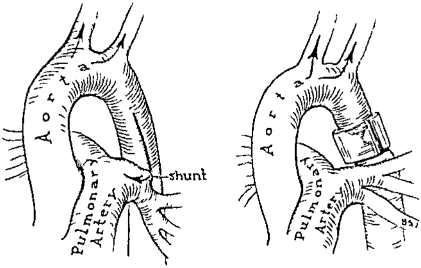
TABLE II. COARCTATION—OPERATIVE SURVIVORS

Follow-up—2 years	
Symptoms—none	
Additional Left-to-Right Shunts	
None	3
Suspected	2
Definite	3
Average Pressure Gradient	
Preoperative	90 mm. Hg
Postoperative	13 mm. Hg

Preoperatively the arm-leg pressure gradient for the survivor group averaged 90 mm. Hg. This has been reduced by operation to 13 mm. Hg, and in 3 the pressures are equal. The highest individual residual gradient is 50 mm. Hg, reduced from a preoperative value of 100 mm. Hg. Technical repair in this case may not be satisfactory, although the child is now 2 years postoperative, and as yet is manifesting no brachial hypertension.

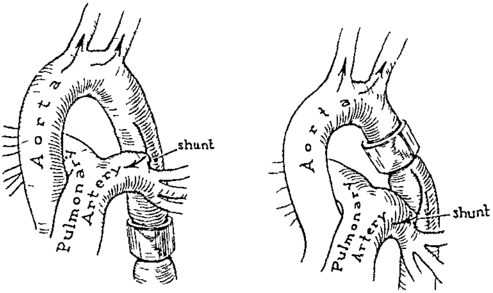
The electrocardiogram pattern and the cardiac contour have reverted to normal in the 3 cases with no residual defects. In the 2 suspect cases, a suggestion of right ventricular enlargement remains by both electrocardiogram and chest film, although there has been definite improvement over the preoperative state. In the 3 children with definite additional defects, there has been marked improvement in the clinical condition, but the electrocardiograms are unchanged, and the chest roentgenograms look very little different, except for a decrease in pulmonary vascular congestion.

We plan to follow the 5 children with possible additional defects closely for the next few years, and perform diagnostic angiocardiography when indicated. In all probability, at least 3 will require open heart repair. All 8 children will be followed through the growth years to obtain accurate information concerning the problem of relative stenosis at the suture line.



Patent ductus arteriosus

Coarctation



Postductal coarctation
and Patent ductus arteriosus

Preductal coarctation and
Patent ductus arteriosus

Fig 6.—Shows the four types of experimental preparations employed in the study of coarctation and patent ductus.

EXPERIMENTAL STUDIES

The hemodynamic alterations that occur with isolated aortic coarctation or patent ductus arteriosus have been amply studied both clinically and experimentally, but investigation of the changes that occur with the two lesions in combination have not been reported. To answer some of the puzzling questions that have come up while caring for these infants, the following long-time experiments were done: appropriate base line data, including carotid and femoral arterial pressures, right heart catheterizations, chest roentgenograms, and electrocardiograms were obtained in a number of dogs, and then four categories of experimental animals were prepared. These were: (1) patent ductus only—4 dogs, (2) coarctation only—4 dogs, (3) patent ductus and postductal coarctation—8 dogs, and (4) patent ductus and preductal coarctation—7 dogs (Fig. 6). The aorta-pulmonary artery shunts were all of the Potts type, constructed as near 5 mm. in length as possible. Gradually progressive coarctations were produced by the use of cylinders of Ameriod plastic encased in stainless steel jackets, a method described by Berman.[11] Total occlusion of the aorta occurs with this method in 2 or 3 months. Dogs of uniform size and weight were used to facilitate comparison between groups. The animals in each group were then followed, and the base line studies repeated at intervals until death or sacrifice. Ninety-three complete sets of postoperative observations were done in the 23 dogs, an average of four observations per dog. Complete autopsy studies were done by a member of the Pathology Department.

Results.—Group 1 (isolated patent ductus) and Group 2 (isolated coarctation) were used as controls. Each lesion was tolerated exceedingly well (Table III). In Group 1, a loud continuous murmur was present in all 4 dogs, and they remained asymptomatic until sacrificed (average 7 months). The animals in Group 2 likewise remained vigorous and healthy. All developed a pronounced collateral circulation. One dog died of a ruptured aorta at the site of the ring at 50 days, and the remaining 3 were sacrificed, 2 at 5 months and 1 at 15 months. No dog in either group developed roentgenographic or electrocardiographic changes of significance.

Table III. Fate of Experimental Animals

	LIVED	DIED
Patent Ductus	4	0
Coarctation	3	1
Postductal	3	5
Preductal	0	7

The clinical course of the animals in Groups 3 and 4 was quite different. In Group 3 (patent ductus with postductal coarctation) 4 of the 8 dogs developed the signs and symptoms of cardiac failure, with dyspnea, tachycardia, pulmonary congestion, ascites, and edema. Cardiomegaly was present. There was no response to digitalis therapy, and they died 2, 4, 6, and 36 weeks after operation. A fifth animal died of aortic rupture. The other 3 dogs remained asymptomatic, in spite of a functioning ductus and an evident coarctation, until they were sacrificed 1 year postoperatively. In Group 4 (patent ductus and preductal coarctation) the combination of lesions was the least well tolerated. All 7 animals developed severe congestive failure. Survival time varied from 13 days to 56 days (average 39 days). Chest films showed a pronounced degree of cardiomegaly and vascular engorgement. A few animals in Groups 3 and 4 developed questionable right ventricular enlargement by electrocardiogram.

Fig. 7 shows the blood pressure response to the various procedures. Two values are shown, the preoperative and the final observation before death or sacrifice. Although the spread of mean pressures was moderately large, the directional trends are accurate, for no animal had a pressure response opposite to that depicted for his group With patent ductus, mean carotid pressure was maintained while mean femoral pressure fell In isolated coarctation, mean carotid pressure was elevated while the femoral pressure remained

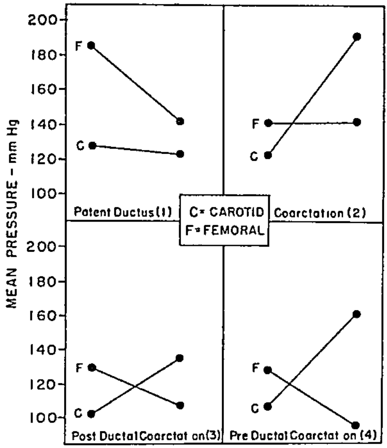


Fig 7—Shows the systemic pressure response to the various operative procedures (Description in text)

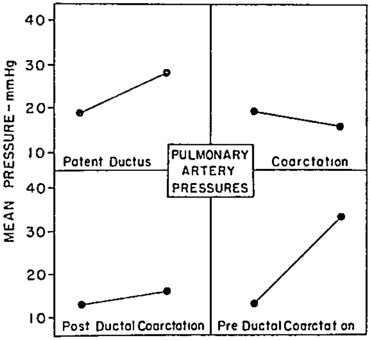


Fig 8—Shows the pulmonary artery pressure response to the various operative procedures (Description in text)

the same In Groups 3 and 4, in spite of a different spatial relationship between coarctation and shunt, the over all response was the same, a rise in mean carotid pressure and a fall in mean femoral pressure Fig 8 shows the pulmonary artery pressure depicted in the same way In Groups 1, 2, and 3 the operative procedure had no significant effect, while in Group 4 (preductal coarctation) mean pressure was elevated to 33 mm. Hg. Right ventricular diastolic pressures were never significantly above the zero level in any group.

Autopsy examination of animals dying in failure revealed edema, pleural effusion, pulmonary and hepatic congestion. Collateral circulation was most pronounced in isolated coarctation, less so with the combined lesions. Measurements of right and left ventricular wall thickness showed a pronounced degree of left-sided hypertrophy with isolated coarctation, less when a ductus was also present. Right ventricular thickness was essentially the same in all groups, but the dogs in Group 4 had right ventricular dilatation in addition. Study of the lungs revealed small vessel thrombi and intimal proliferative changes to a moderate degree in Groups 3 and 4, but these findings were not pronounced.

DISCUSSION

A significant clinical experience with aortic coarctation complicated by patent ductus arteriosus has convinced us that this combination is a most malignant one, and unless vigorous treatment is instituted almost from birth, the mortality will approach 100 per cent. We are also of the conviction, on the basis of our discouraging experiences with medical therapy alone, that early corrective surgery must be done, even in the face of congestive failure in a critically ill child, if any number are to be saved. Our surgical results will bear improving, 56 per cent survival in 16 cases, but an encouraging upward trend has been seen in the last 5 years, when there have been only 2 deaths in 11 cases, a survival rate of 82 per cent. Early detection of cases and better anesthetic techniques have contributed greatly. For early diagnosis the condition must be kept in mind, for the infants have a variety of nonspecific symptoms. The flush blood pressure technique has been of immense help.

Attempts to separate these infants into various categories on the basis of clinical or laboratory findings had proved futile for us. Some clinicians rely heavily on the electrocardiogram, believing those children with left ventricular enlargement have less serious lesions and can be managed medically, while those with a right-sided pattern have a graver prognosis, a greater probability of additional shunts, and will usually die unless helped surgically.[3, 9] In our experience, the electrocardiogram pattern has not been this reliable. Table IV shows the relationship between the electrocardiogram, ductus position, and associated defects in this series. Right- and left-sided patterns were found with both anatomic variations of ductus position, and with and without additional left-to-right shunts. We believe that selection of cases for operation should be based on the diagnosis of significant coarctation in any infant exhibiting cardiac failure and cardiomegaly, without regard for the electrocardiogram pattern. In virtually all such cases a patent ductus will be present with the coarctation.

Two objections have been raised to the correction of coarctation in infancy. One is that the mortality will be prohibitively high should an intracardiac lesion also be present. We take the opposite view, and feel that the only plausible method of management is the prompt correction of the coarctation and division of the ductus, making it possible to defer repair of the intracardiac component to a later time. As yet we have no children carried through the second phase of this plan, but there are 3 in the group that will almost surely need further surgical attention. The other objection relates to the development of a relative coarctation at the line of anastomosis with body growth. No absolute data are available as the follow up in the reported cases is still too short. Moss and his co workers[12] have recently reported angiographic studies on 5 infants followed 2 to 4 years after repair, and concluded that after proper corrective surgery the aorta should remain functionally patent regardless of growth. In any event, it is evident that surgery in infancy is lifesaving, and even if reoperation is necessary during adolescence, this is still an equitable price to pay.

TABLE IV RELATIONSHIP OF DUCTUS POSITION, ECG, AND ASSOCIATED DEFECTS IN 16 CASES OF COARCTATION AND PATENT DUCTUS

CASE NO	DUCTUS POSITION	ECG PATTERN	ASSOCIATED DEFECTS	OPERATIVE OUTCOME
1	Preductal	RVE	None	Died
2	Preductal	RVE	None	Died
3	Preductal	LVE	None	Died
4	Preductal	RVE	None	Died
5	Preductal	RVE	VSD	Died
6	Juxtaductal	LVE	None	Survived
7	Preductal	LVE	Fibroelastosis	Died
8	Preductal	RVE	Left to right shunt	Survived
9	Preductal	RVE	None	Died
10	Juxtaductal	LVE	None	Survived
11	Preductal	RVE	?Left to right shunt	Survived
12	Juxtaductal	LVE	?Left to right shunt	Survived
13	Juxtaductal	LVE	None	Survived
14	Juxtaductal	LVE	Left to right shunt	Survived
15	Preductal	RVE	Ostium primum	Survived*
16	Juxtaductal	RVE	Left to right shunt	Survived

*Died 9 months later

Very little is known about the precise hemodynamic alterations which make coarctation and patent ductus such a serious combination. Gupta,[13] in acute animal experiments, demonstrated that the opening of a ductal shunt distal to a coarctation makes the constriction physiologically more severe. Thus, the femoral pressures and pulse contours with a 65 per cent coarctation and open shunt resemble those of an isolated coarctation of 75 per cent. This is an important concept if it applies to human cases. It is difficult to believe that the alleged lack of development of collateral channels in the preductal group has much to do with the prognosis. Such channels are actually demonstrable at autopsy in many cases.[2] Clinically it is rare to find an infant with differential cyanosis of the lower trunk, indicating maintenance through the ductus by a "systemic" right ventricle. None of our patients had differential cyanosis, and oxygen saturations done in a number showed no difference above and below. Edwards[14] was the first to call attention to the vascular obliterative disease to be found in the lungs of these infants, and others since have commented on the severe pulmonary hypertension that is present when such measurements can be made.[9, 12] Although the pathogenesis of the hypertension, and the exact relationship between it and the observed vascular changes are not yet worked out, it is most likely that the pulmonary vascular tree plays a major role in influencing the clinical picture of coarctation and patent ductus, just as it does in so many other congenital malformations (Fig. 9).

Our animal observations are pertinent to these problems. Under experimental conditions the combination of coarctation and patent ductus was also poorly tolerated, whereas the isolated lesion caused little or no difficulty. Cardiac decompensation occurred regardless of the relative position of the shunt to the constriction, although it appeared that the preductal arrangement was the more serious one, and in this group pulmonary hypertension was seen. A well-developed collateral circulation did not prevent heart failure. Like its clinical counterpart, the failure responded very poorly to digitalis therapy, and the animals died in spite of vigorous medical treatment. At autopsy, early obliterative changes were seen in the small pulmonary vessels, and, in the preductal group, dilatation of the right ventricle indicated that there was considerable strain on this chamber during life.

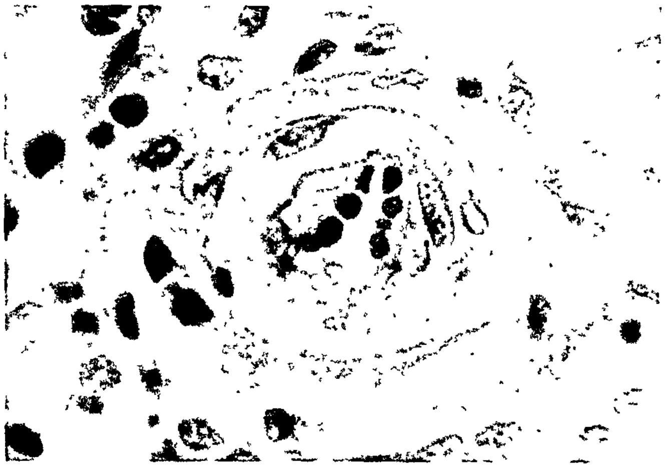


Fig. 9.—Small pulmonary arteriole from an infant with coarctation and patent ductus. The muscular layer is greatly thickened. In comparable vessels from the lungs of normal infants of this age the muscular layer is virtually absent.

SUMMARY

1. Sixteen infants with coarctation of the aorta and patent ductus arteriosus treated by early surgical correction are presented. Clinically all were in refractory cardiac failure, and had marked cardiomegaly. The electrocardiogram pattern was variable. Diagnosis was made by demonstrating a significant pressure gradient by the flush technique.

2. Median age at the time of operation was 6 weeks. Wide anatomic variation in the relationship of the two lesions was encountered. Operative

mortality was 44 per cent for the series In the last 5 years there have been 11 cases with only 2 deaths

3 There has been 1 late death The other 8 children have been followed an average of 2 years All are asymptomatic Clinically, several have additional intracardiac shunts which will require closure in the future

4 We are of the conviction, on the basis of this experience, that prompt correction of the coarctation and division of the ductus is the only rational form of treatment for these seriously ill infants

5 Observations are presented which demonstrate that coarctation and patent ductus is also a lethal combination in the experimental animal

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(For Discussion, see page 85)

PROBLEMS IN THE SURGICAL MANAGEMENT OF COARCTATION OF THE AORTA

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DEFINITIVE resectional surgery for coarctation of the aorta was introduced 15 years ago.[1,2] During the ensuing years, thousands of patients have been successfully operated upon and the surgical technique has become well standardized. Today, the operative mortality is very low and, in general, the mere diagnosis of coarctation is in itself clear and sufficient indication for surgery. Despite these facts, coarctation of the aorta is not completely understood and retains problematical therapeutic aspects. These problems may appear during the operation or in the postoperative period and, as will be shown in this paper, they usually can be solved without jeopardizing the life of the patient. However, these problems raise questions concerning surgical judgment and the requisites of a satisfactory surgical result. We do not venture to offer definitive solutions to these problems but, rather, in this paper, we present our findings with the object of stimulating worthwhile discussion that ultimately should benefit future patients with coarctation.

SURGICAL EXPERIENCE

Our surgical experience with coarctation to January, 1959, includes 60 patients, all operated upon within the past decade. There have been 7 operative deaths and in 1 patient no definitive operation was accomplished. It will be seen from Fig. 1 that this is a safe operation, if the extremes of age in the life history of the disease are avoided. The two deaths in the middle-age span occurred in (1) the first patient in the series who died of a delayed anastomotic leak, and (2) the only patient in the series in whom it was attempted to swing down the very large subclavian artery for end-to-end anastomosis below the coarctation. The technique worked nicely; however, the patient died suddenly approximately 6 hours after operation. The crotch between the aorta and the subclavian artery had split open where it had been hyperextended. Pathologically, there was found to be a loss of elastic tissue in this region. This experience led us to avoid using this method and certainly nowadays the use of grafts has rendered this technique obsolete.

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The problems that have been encountered in this operative experience may be broadly grouped under five headings (1) coarctation diagnosed in patients 1 year of age or less, (2) coarctation diagnosed in patients more than 45 years of age, (3) the syndrome of postoperative abdominal pain, (4) the size of the anastomosis, and (5) residual hypertension

1 *Patients 1 Year of Age or Less*—Eleven patients 1 year of age or less have been operated upon for coarctation This seems like a high percentage of our total operative experience and is probably not a true indication of the relative frequency of significant symptoms in this age group It reflects both an active pediatric cardiological service and pediatricians alerted to the significance of feeling the femoral pulsations All 11 patients manifested congestive heart failure (Table I)

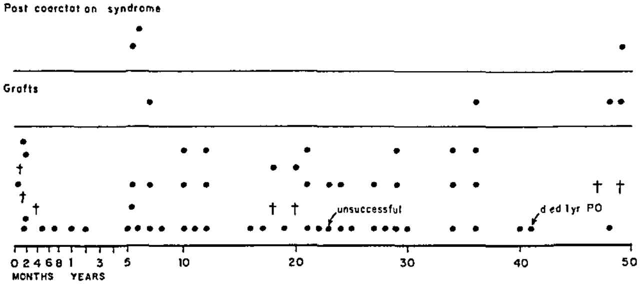


Fig 1—Summary of the operative experience upon which this paper is based The ages of all 60 patients are indicated at the bottom of the figure Details of the 7 operative mortalities are discussed in the text. The patient designated unsuccessful had an aneurysm distal to the coarctation This was early in our experience grafts were not available and no accomplished The patient who died 1 year following surgery died atic heart disease All of the other patients are known to be living chart shows that grafts were used in only 4 of the 60 patients The pain syndrome was recognized on only 3 occasions

An important question that remains to be definitely settled regarding the advisability of this operation on infants is whether they will "outgrow" their anastomoses and relative coarctation will recur The precaution of using interrupted suture technique should be followed because such anastomoses have grown well experimentally, but the possibility of the recurrence of coarctation is an important theoretical objection to performing this operation electively on infants[3] [4] In this regard, our longest postoperative follow-up is only 4 years and there is no clinical evidence of recurrent coarctation at the present time Others undoubtedly have additional evidence on this point

In a recent paper, Moss and associates[5] on the basis of five postoperative angiographic studies, suggest that growth of anastomoses lags relative to normal infantile aortas However, in our experience many of these aortas are definitely abnormal (hypoplastic) Furthermore, it may be technically impossible in minute aortas to perform an "ideal" anastomosis that leaves

TABLE I. TABULAR SUMMARY OF [illegible]TIENTS OPERATED UPON 1 YEAR OF AGE OR YOUNGER

NAME	AGE	SEX	CLINICAL ASPECTS	CATHETERI[illegible] FINDINGS	OPERATIVE FINDINGS	POSTOPERATIVE COURSE	COMMENT
K. O.	3 wk.	M	Cyanosis, tachycardia, cong. fail., and Wolff-Parkinson-White syndrome	Not catheterized	Typical + PDA, cardiac arrest	Benign; good femoral pulses	
S. S.	5 wk.	M	Cyanosis, cardiomegaly, cong. fail.	Coarctation, IASD, ? PDA	Typical, small PDA	Benign; subsequent oper. for mediastinal mass (hyperplastic thymus)	Postop. catheterization, femoral artery pressure rose from 45/37 to 110/70
P. L.	5 wk.	F	Dyspnea, cyanosis, cong. fail.	Coarctation, PDA, IVSD	Hypoplastic arch, big PDA, systemic PA pressure did not fall on dividing PDA	Resp. failure and cardiac arrest 2nd postop. day, resuscitated; died 3 wk. postop.	Autopsy; Eisenmenger
D. N.	6 wk.	F	Cyanosis, tachypnea, cong. fail.	Coarctation, ? lt.-to-rt. shunt	Atresia of aortic arch, PDA supplied descending aorta	Died after surgery	Autopsy; atresia from innominate to subclavian, subaortic stenosis, IVSD, PDA
D. W.	7 wk.	M	Cyanosis, dyspnea, cong. fail.	High coarctation with hypoplasia of arch	Coarctation at subclavian wedge resection	Benign; progressive decrease in heart size	
K. Y.	7 wk.	M	Dyspnea, cong. fail.	Coarctation, ? myocardial disease	Typical, hypoplastic arch	Benign; decreased heart size	
B. W.	2 mo.	F	Cardiomegaly, cong. fail.	Coarctation, hypoplastic arch, IVSD	Typical, much collateral, distal arch hypoplastic	Benign; relative narrowing at anastomosis	Postop. catheterization, femoral pressure rose from 70/46 to 102/60; no residual shunt detected
J. A.	4 mo.	M	Dyspnea, cong. fail.	Coarctation, IVSD, pulm. hypertension	Small PDA, hypoplastic aorta, coarctation not recognized	Died postop.	Autopsy; coarc. in hypoplastic segment, IVSD
M. E.	5 mo.	M	Grand mal, cong. fail.	Coarctation, PDA above intracardiac lt.-to-rt. shunt	Typical	Benign; IVSD closed 6 mo. later	Femoral pressure: preop. 64/72—postop. 98/56
N. G.	7 mo.	F	Tachypnea	PDA, IVSD (coarctation missed)	Large PDA, very small proximal aorta	Benign; heart size ⅓ smaller	Postop. catheterization, rt. vent. pressure fell from 89/3 to 40/7; residual narrowing in hypoplastic segment
W. W.	1 yr.	M	Poor development, pulm. congestion, cardiomegaly	PDA (coarctation missed)	PDA, coarctation below diaphragm excised, Heineke-Mikulicz repair	Benign; heart smaller	

PDA = patent ductus arteriosus; IVSD = interventricular septal defect; IASD = interatrial septal defect.

no local deformity. Under such circumstances, normal findings on postoperative studies must be exceptional. Fortunately it is function and not appearance that counts and none of their re-studied patients had residual pressure gradients.

With the recent rapid development in pediatric cardiology, it has become apparent that coarctation is a significant cause of left heart failure in infancy. It is our current belief that, if these infants do not respond promptly and completely to anticongestive measures, surgery offers less risk than protracted medical treatment. In the accompanying chart (Fig. 2) there is evidence that these infants get into difficulty because of associated additional congenital cardiac defects. Seven of the 11 infants were found to have intracardiac left-to-right shunts; 2 others had only extracardiac shunts (patent ductus); each of the 3 patients who did not survive surgery had a large interventricular septal defect with systemic pulmonary hypertension. These findings indicate that the coarctation may be the straw that breaks the camel's back. Hopefully, correction of the coarctation may be lifesaving and allow future correction of the other anomalies. Subsequent studies on 2 survivors with intracardiac shunts revealed dramatic improvement. One lost all catheterization evidence of an interventricular septal defect. This suggests that a fall in left ventricular pressure may allow a small shunt to close. In a second patient, who also had a large patent ductus immediately above the coarctation as well as an interventricular septal defect, the right ventricular pressure fell from 89/3 to 40/7 mm. Hg. This relationship of coarctation and ductus may result in extreme pulmonary hypertension. A third infant, 5 months old at the time

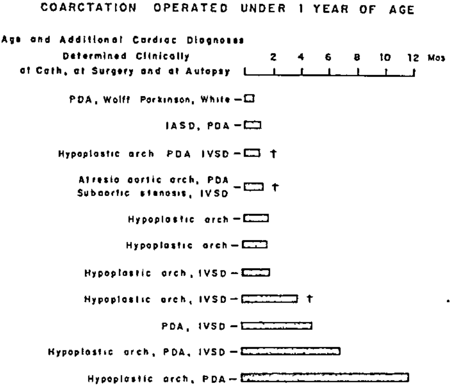


Fig. 2.—This figure emphasizes the large number of associated cardiac defects in infants having symptomatic coarctation. Seven of the 11 patients had associated intracardiac shunts and 2 additional ones had patent ductus arteriosus. In all, there were 7 patent ductus. In 8 of the 11 cases there was hypoplasia or atresia of the aortic arch system. The 3 patients who died as a result of operation had palpably systemic pulmonary hypertension, and, in all 3, including the 2 with patent ductus, this pressure did not fall as a result of the operative procedure.

of division of his coarctation, retained systemic pulmonary hypertension due to an interventricular septal defect. This was closed by open cardiotomy 6 months later, and he has done well since.

In the adult coarctation there often is hypoplasia of the proximal aortic segment. This is also seen in the infant in whom this segment may seem extremely small (Figs. 3, 4, 5). Under these circumstances, in 2 infants it was impossible from the outside of the aorta to suspect that, in addition, there was a diaphragmatic obstruction typical of coarctation. In the first of these patients, a patent ductus was divided and, although coarctation was suspected from contrast studies at catheterization, no aortic resection was done and the coarctation was proved at necropsy on the following day. On the basis of this experience, the second case was recognized and treated properly. Frequently the coarctation deformity of infancy is less obvious than that seen later in life. It is likely that the coarctation represents a point of fixed narrowing and with growth the adjacent aorta enlarges to give the typical hourglass deformity. It is suggested that when in doubt the suspected segment of aorta should be longitudinally incised so that, if a coarctation is not found, the aorta can be reconstituted. However, each time we have done this, the longitudinally incised segment has been excised as a part of the coarctation specimen with the exception of 1 patient in whom it was believed wise, because of the small caliber of the vessels involved, to treat the coarctation by closing the incision in Heineke-Mikulicz fashion after excising the diaphragm. The only other unorthodox anastomotic procedure was in another extremely hypoplastic aorta in which the anterior two thirds of the coarcted segment was excised as a transverse wedge and an end-to-end anastomosis was done in the usual fashion, except that the posterior portion of the aorta remained intact.

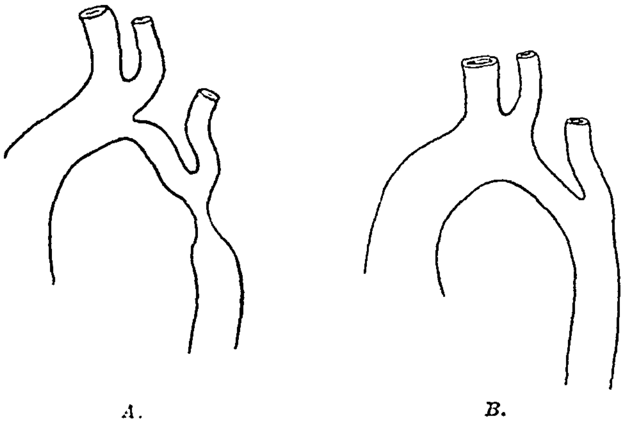


Fig. 3.—Tracings of enlargements of single frames of 35 mm. motion-picture film on 2-month-old infant B. W. *A* depicts the preoperative status. *B* is from a selective angiocardiogram done 1 year postoperatively. On the basis of the extremely hypoplastic distal arch depicted in *A*, it was suggested that this patient might well prove to have a surgically hopeless problem. Note that there is no residual anastomotic narrowing, but that a definite relative hypoplasia in the distal aortic arch persists. The femoral artery pressure to direct measurement at the time of the studies (*A*) was 70/46; at the time of the studies (*B*) it was 102/60.

The infant who has a hypoplastic proximal segment, be it a long portion of the arch or only the segment from the subclavian to the coarctation, will, of course, have an anastomotic lumen no larger than this segment. This may be only one fourth or one third the diameter of the descending aorta beyond the anastomosis. We have several postoperative studies which suggest that this size discrepancy persists (see Figs. 3, 4, 5). Application of Bernoulli's principle to such a system reveals that the pressures are such that the narrowing may conceivably be self perpetuating (Fig. 6).[6, 7] Nevertheless, the 3 surviving patients in whom this size discrepancy was most marked have done well, recovered from heart failure, and do not need digitalis.

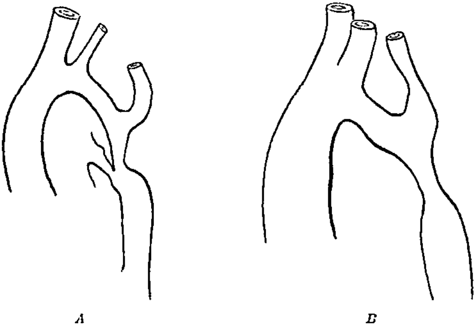


Fig 4—Tracings of enlarged single frames of 35 mm motion-picture film from infant S S. *A* is a preoperative one, when the infant was 5 weeks old *B* is from studies 7½ months later At the time of surgery, in addition to the patent ductus, there was a diaphragmatic component to the coarctation situated at the narrowest point shown This could not be seen on the angiographic studies due to insufficient contrast Note that in the postoperative study the relative hypoplasia of the proximal aorta persists essentially unchanged Directly measured femoral artery pressures at the time of these two studies were 45/37 and 110/70, respectively

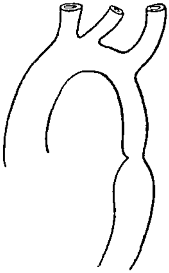
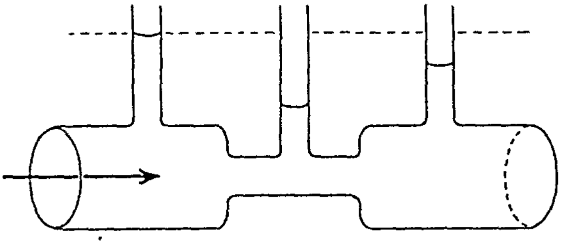


Fig 5.—Postoperative angiographic study traced from an enlargement of a 35 mm motion-picture frame on Patient N G The child was 2 years of age at this time and the study was made 16 months after surgery At the time of surgery, the operator commented upon the very small size of the proximal aorta There was also a very large patent ductus arteriosus Certainly the relative hypoplasia has persisted Residual anastomotic deformity of this degree is probably not hemodynamically significant, but this child should certainly be restudied in several years to see if the deformity increases with growth

The anatomy of coarctation in the infant is highly variable. However, the only striking difference between infants and adults lies in the group of patients with long segments of narrowing, or even atresia, of the aortic arch. These patients with so-called "infantile" types of coarctation do not often survive to be seen as adults. We ordinarily obtain angiographic demonstration of coarctations only in exceptional cases; particularly in the adult group with grafts readily available. However, all but 1 of the 11 infants were catheterized and, in most, selective angiocardiograms also were obtained. In view of the high incidence of associated defects we now believe such study usually is indicated. But too much reliance should not be placed on unfavorable angiographic pictures of the aortic arch, and almost without exception the infant with coarctation in heart failure should be explored. Although the use of grafts does not seem practical, 2 patients survived operation who were believed to have inoperable conditions on the basis of angiographic studies; the coarctations were not as proximal or as long as predicted.



BERNOUILLI'S PRINCIPLE

Fig. 6.—Most readers will recall a comparable drawing in their textbook of high school physics. Stated in its simplest terms, the principle is that in any fluid system greater speed of flow is associated with lower pressure. In the tubing depicted above with a constant flow of fluid going from left-to-right it is obvious that the fluid travels faster through the "coarcted segment." The pressures are measured in the manometers taking off from the various portions of the tubing. A more refined example of Bernoulli's principle is the airplane wing in which case air has to travel farther to pass over the curved upper surface than the flat bottom surface; therefore speed is greater, and pressure lower above the wing, and the wing thus acquires lift. If, in the system depicted, the narrowed segment is made out of soft rubber, one will find that as the flow is increased the soft segment can be made to collapse together, indicating a pressure lower than the surrounding atmospheric pressure.

2. *Coarctation in Patients More Than 45 Years of Age.*—The commonest causes of death in patients with untreated coarctation of the aorta are complications of degenerative vascular disease, either closely related to the coarctation itself or in the cerebral circulation. Obviously the tendency to premature development of arteriosclerotic and other degenerative vascular changes increases the operative risk with advancing years, but it is not rational to set a hard and fast age deadline beyond which coarctations should not be resected. The 3 oldest patients in this series were 47, 48, and 49 years of age, respectively. The 47-year-old patient had an uneventful operation, although the aorta was extremely friable and held sutures poorly. She was readmitted to the hospital 3 weeks following operation with fever, dysphagia, and hoarseness, and died shortly after this with a mycotic false aneurysm at the anastomotic site. The 48-year-old patient required a graft for anatomic

rather than degenerative reasons and has had an uneventful postoperative course for more than 1 year The 49 year old patient presents an interesting problem and will be briefly discussed

A 49 year old white man had been aware of high blood pressure since the age of 11 years At the age of 36 years 13 years prior to examination here he had a cerebral vascular accident with transient left hemiplegia At this time the diagnosis of coarctation was established In the interim, the patient had led a moderately sheltered existence and stated that his blood pressure had ranged from 230/120 to 260/120 mm Hg Within the 3 months prior to being examined here, the patient had noted the onset of progressive dyspnea, paroxysmal nocturnal dyspnea, and a nonproductive cough During this time he developed auricular fibrillation and was digitalized Hospitalization was precipitated by the progression of his symptoms in spite of treatment Under hospital conditions it was not difficult to control his congestive failure Blood pressure was reported at from 250/80 to 290/110 mm Hg in the arms No blood pressure and only equivocal pulses could be detected in the legs It seemed clear that this patient had little future without surgery and the patient elected to undergo operation after frank discussion

The coarcted segment was resected A 5 cm homograft was used chiefly to get beyond atherosclerotic changes that were maximal in the immediate vicinity of the coarctation The operative procedure was uneventful Early in the postoperative period the blood pressure in the upper extremities fell to approximately 140/90 mm Hg (Fig 7) At this blood pressure, the patient had a rapid, weak pulse, was cold to the touch, and covered with profuse perspiration He presented the typical picture of deep surgical shock in spite of a "normal" blood pressure His condition did not respond adequately to blood transfusion and vasopressor agents On the first postoperative day he was placed in a "G suit"[8] which compressed his body from the waist down The systolic blood pressure was easily maintained at approximately 180 The patient lost his appearance of shock and felt well subjectively During the next 16 hours, whenever the 'G suit" was deflated, the patient's pressure fell and the shock-like state recurred Four days postoperatively the clinical picture progressively improved and the blood pressure stabilized at 190/90 in the upper extremities with a pressure in the legs of 175/80 Six days postoperatively, the picture became complicated by abdominal pain and distention of an ill defined nature and mental confusion This confusion and mildly progressive abdominal symptoms and signs continued until death in coma occurred on the eighth postoperative day

Necropsy showed severe arteriosclerosis in the remaining aorta and in both the cerebral and coronary arteries There was extensive recent encephalomalacia in the right cerebral hemisphere Also noted were three berry aneurysms in the middle cerebral arteries An additional finding which will be discussed subsequently was a necrotizing angiitis of the "acute, hypersensitivity type" that was evident in colon, renal arteries, and prostate

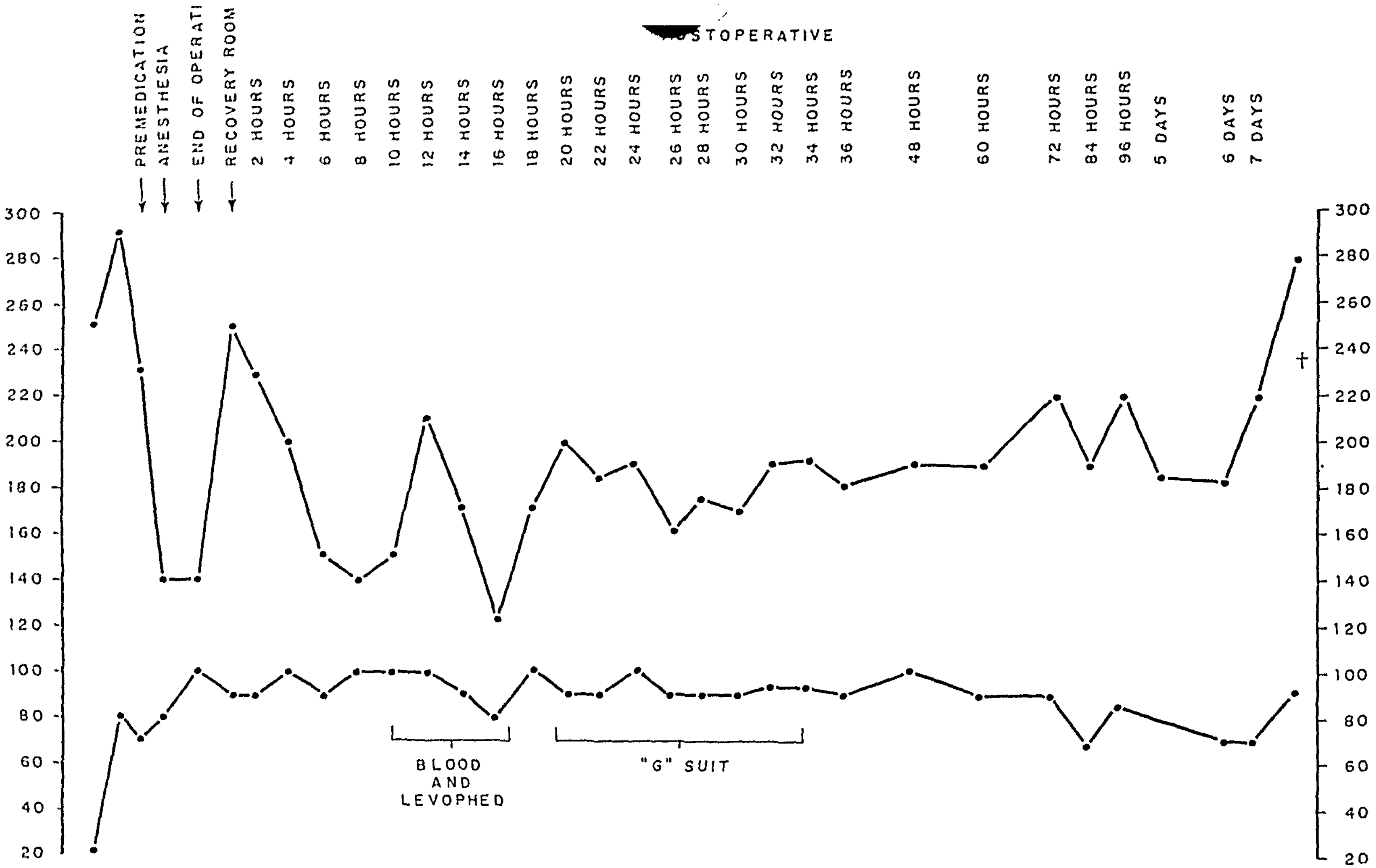


Fig. 7.—Graphic summary of systolic and diastolic blood pressure in Patient H. B., aged 49 years. Note that there was no stability to his postoperative blood pressure until the G-suit was applied, approximately 16 hours after surgery. During the period depicted, the clinical course and necropsy findings proved that the circulation maintained was inadequate to perfuse large portions of the brain.

In brief, this man died as a direct result of inadequate cerebral perfusion at the lowered postoperative blood pressure No discrete vascular occlusions could be demonstrated in the cerebral circulation The only finding was advanced arteriosclerotic changes with resultant severe narrowing Paradoxically the situation resulted in which the cerebral circulation would not tolerate the lowering of blood pressure associated with a technically satisfactory operation Admittedly this case is an isolated occurrence in our series However, it is a readily explainable complication and theoretically may occur with some frequency in patients of this age group We should be interested to know if others have encountered similar problems

3 *Syndrome of Postoperative Abdominal Pain*—The syndrome of abdominal pain following surgical resection of coarctation occurs with sufficient frequency so that most thoracic surgeons have observed it Sealy[9] first mentioned such a case in 1953 and described what has proved to be the typical pathologic picture Other case reports followed,[10] [11] but it remained for Ring and Lewis[12] to assemble a group of these cases and forcefully bring to the attention of thoracic surgeons the true significance of this problem A group of poorly understood and presumably coincidental postoperative abdominal complications suddenly made sense and were obviously thereafter better cared for

The incidence of this problem may be surprisingly high Ring and Lewis[12] report some degree of the syndrome in 28 per cent of 64 postoperative patients It is difficult to draw the line between more than the usual postoperative distention and ileus and a true abdominal complication A review of our records revealed only 4 clear cut examples of worrisome postoperative abdominal problems in 60 cases, and 1 of these proved to be an unrelated condition

It seems clear that the basic pathologic lesion is a mechanically induced panarteritis in the visceral arterial tree The mechanical insult is related to the increased pressure head and pulsation resulting from relief of the obstruction in the aorta Comparable vascular lesions have been experimentally produced in the kidneys of rats, in which animals the splanchnic circulation is apparently relatively more resistant[13] The renal arteries of the 49 year old man cited above did show such changes at necropsy Renal arterial changes may well be common after operation for coarctation, but do not manifest themselves as overtly as do changes in the mesenteric circulation Sealy and associates[14] state that their experience suggests that the abdominal pain syndrome occurs in those patients who have a reactive hypertension of greater than preoperative levels occurring after the second postoperative day, and lasting for from 1 to 2 weeks In a few patients, we have observed and have been quite concerned about this type of reactive hypertension, however, these individuals have not shown the abdominal pain syndrome* It is possible,

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*In a 5 month old infant operated on too recently to be included in this series the syndrome appeared in the presence of definite reactive hypertension (blood pressure up to 150/100 mm Hg) On Apresoline therapy, the course was uneventful

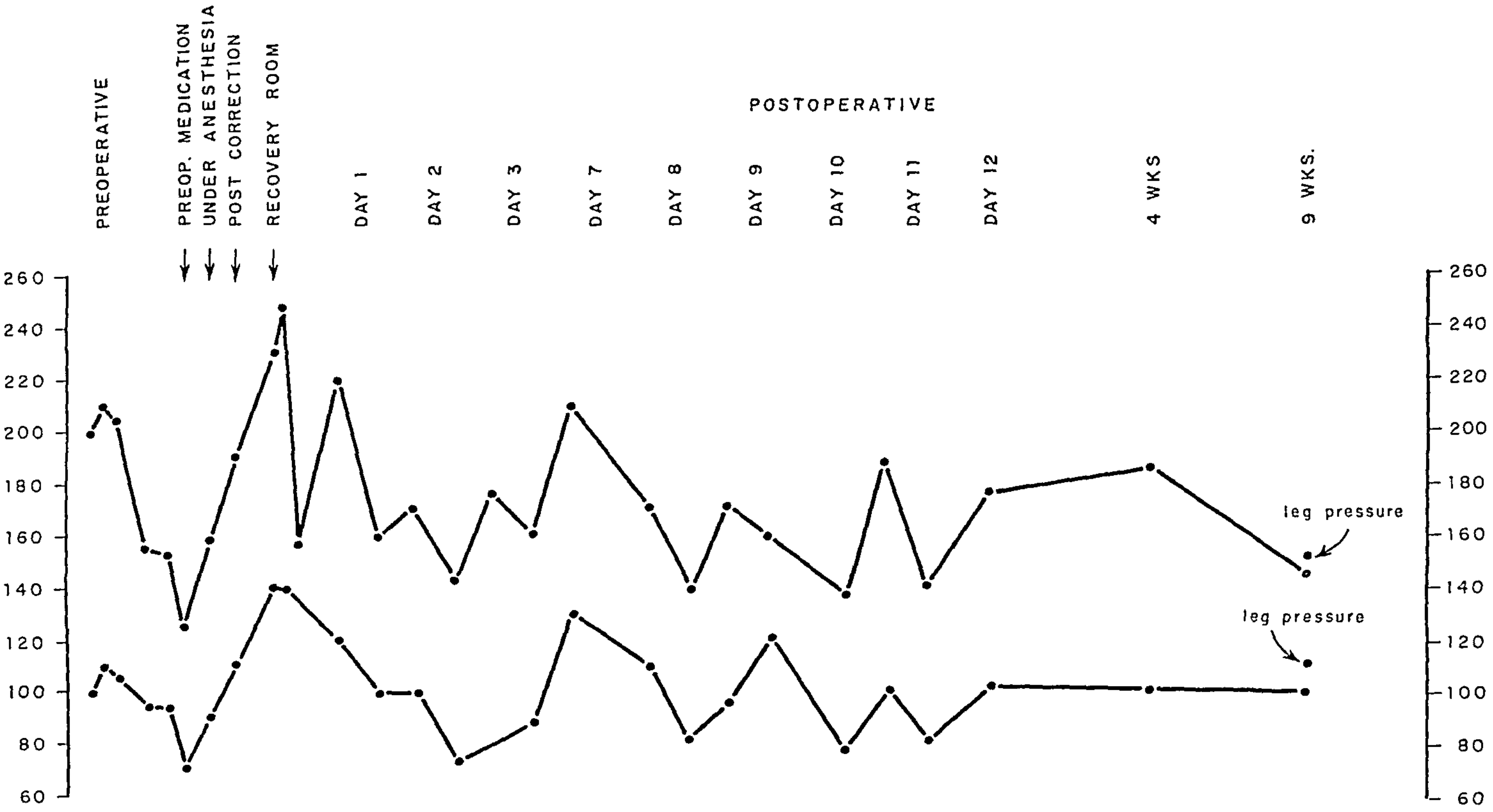

Fig. 8.—Example of reactive postoperative hypertension seen in a 23-year-old woman, V. G. Note that her preoperative blood pressure was quite labile; however, prior to surgery it had subsided to approximately 150/90. Note that 9 weeks were required after surgery before the pressure has returned essentially to these levels. This picture is common after surgery for coarctation of the aorta; however, except for the infant mentioned in the footnote, we have not recognized the abdominal pain syndrome associated with it. The hypertension causes the surgeon concern about the anastomosis, but to date such concern has been unfounded in our experience.

however, that reactive hypertension is related to acute postoperative renal vascular changes (Fig 8) Two children who had the syndrome of postoperative abdominal pain in its classic form had no dramatic fall in blood pressure in the immediately postoperative period, but, in each, the systolic pressure was essentially unchanged from the preoperative level during the first postoperative week In the third patient, the 49 year old man already reported, the fall in blood pressure was immediate and rather dramatic However, it has seemed to us that in all three of these instances a complete relief of obstruction was accomplished with absolutely no anastomotic narrowing or associated aortic hypoplasia and thus the mesenteric arterial tree received maximal increase in blood flow This, of course, is a common operative accomplishment

One of the 2 children with the typical syndrome was a 6 year old boy who had uneventful resection of a typical coarctation He first complained of abdominal pain on the third postoperative day At that time the diagnosis of intussusception was considered, a barium enema study was performed and the examiner thought that he saw and reduced an intussusception However, the same clinical picture of abdominal pain of fluctuating severity with a paroxysmal component persisted There were no true localizing signs The leukocyte count approximated 20,000 per cu mm On the eighth postoperative day, a rather severe exacerbation of abdominal pain with some localization to the right side occurred and a laparotomy was performed The significant findings were injection of the mesenteric vessels in the mid portion of the small intestine with mesenteric lymphadenopathy There was a small amount of soapy fluid within the abdominal cavity Biopsy of the mesentery and a mesenteric lymph node, not including significant blood vessels, showed chronic inflammation and fibrosis The lymph node showed chronic lymphadenitis Following laparotomy, the patient's condition remained unchanged for 1 additional week after which his symptoms progressively disappeared, undoubtedly in spite of, rather than because of, the nonspecific therapy he had been receiving There have been no difficulties in the ensuing 3 years

The other child was a 5½ year old boy At catheterization, a patent ductus and a coarctation with moderate pulmonary hypertension were diagnosed, and at operation the diagnoses were confirmed The patent ductus was of moderate size and straddled the point of maximum coarctation The operative procedure was uneventful, and he first complained of ill defined abdominal pain on the fifth postoperative day By this time we were familiar with the syndrome and followed him closely There were several other interesting manifestations, including a migrating arthralgia of the lower extremities, and a peculiar deep swelling in the left lumbar muscles The child was treated with steroids which relieved the arthralgia, but the abdominal component continued with a fluctuating severity and by the twelfth postoperative day definite ascites was present There was finally sufficient improvement to allow hospital discharge 1 month after surgery He was examined again 2 months after operation when it was apparent that he was still having abdominal difficulties; the condition at this time resembled partial intestinal obstruction. He was hospitalized and barium studies confirmed the presence of partial small-bowel obstruction for which reason laparotomy was performed. The terminal 2 feet of ileum was involved in an inflammatory mass and upon taking this down there were multiple fistulas between the loops. A small abscess was also present. This bowel was resected and an anastomosis performed. The patient had an uneventful convalescence and pathologic examination of the resected bowel showed ulcerations, fistulas, and a small segment of complete dissolution of continuity of the small bowel. Examination of arteries in the specimen showed only rare, slight intimal proliferation. There was no necrotizing vascular lesion. However, this operation was performed more than 2 months after the initial procedure and presumably the operative specimen represented the end stage of this pathologic process with localized bowel infarction.

The fourth abdominal problem mentioned, which was unrelated to the complication under discussion, occurred in a 7-year-old boy. He had undergone resection and graft replacement of a coarctation and a distal aneurysm. Infected thrombi were present in the aneurysm. After several days of abdominal pain, he required emergency laparotomy for an abdominal catastrophe and associated shock. A spleen, containing multiple infarcts, was found to have perforated spontaneously. This case is cited to warn against overconfidence in expectantly treating such patients. In general, however, the syndrome of abdominal pain is a nonsurgical problem.

Sealy[14] has reported that autonomic blocking agents (hydralazine hydrochloride) are effective. We have not had experience with these agents. One of our patients was treated with steroids with equivocal results, the rationale being that a similar pathologic condition on a hypersensitivity basis may respond to this therapy. It should not be forgotten that these patients may undergo visceral infarction and perforation, and should thus be kept under close surgical scruntiny. Additional reports on specific medical therapy for the underlying vascular lesions should be presented. It is rational that antihypertensive drugs offer specific therapy.

4. *The Size of the Anastomosis.*—The goal in any coarctation operation is resection of the narrowed area and reconstitution of the aorta so that there is a smooth channel without residual narrowing. Unfortunately in many instances this is easier said than done. The typical pathologic feature in coarctation is a rather abrupt narrowing with a definite diaphragmatic component that will usually allow an anastomosis having normal or very nearly normal lumen. However, there are two groups of patients in whom this may not be the case: those having definite hypoplasia of the aorta, and those having a lengthy coarcted segment.

Specific mention of hypoplasia was made in the operative notes of 20 of the 60 patients in this series. The commonest manifestation is the finding of a small aorta above the coarcted segment, and of some degree of post-stenotic dilatation, at least relative to the hypoplastic segment, below the coarcted segment (Fig 9) The small aorta may constitute only the segment below the left subclavian artery or it may include the whole visible arch On occasion the entire thoracic aorta may seem definitely small In either case obviously the anastomosis can be no larger than the diameter of the upper segment and certainly little is to be gained by accomplishing an anastomosis that is larger than the diameter of the distal aortic arch

Patients having a lengthy coarcted segment are rare The segment usually is seen as a long tapering constriction, however, in our experience, invariably at the narrow point there is an additional diaphragmatic component Here one may be obligated to use a graft, but how much less than a normal aortic lumen is acceptable under these circumstances? It has been our practice to try

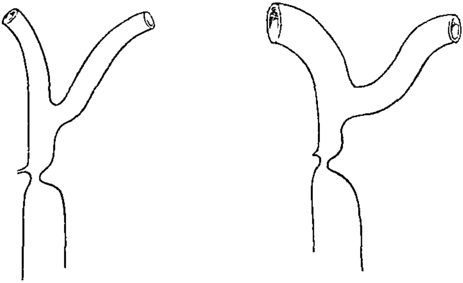

Fig 9 —Drawir s es of hypoplasia in the aortic arch system
Both of these types regularity There can be little justification to
performing a graftin as depicted in *A* An argument can be made
in favor of placing a artery down to the lower segment in *B* In
such circumstances to accomplish an anastomosis with a lumen
of at least 1 cm in to graft

to accomplish the largest anastomosis possible without the use of a graft The reasoning behind this choice has been that, in general, these operations are being carried out on young persons with a life expectancy of many years Since we do not now know the ultimate fate of blood vessel grafts, we have tried to avoid their use when possible This explains the paucity of grafts in this series where they have been used for degenerative or aneurysmal changes associated with the coarctation (Fig 10) Arguments can be made against this approach to the problem These include the possibility of future degenerative changes secondary to the turbulence associated with residual narrowing Also, Rodbard[7] has shown that localized marked reduction in cross section area of a vessel may be followed by intimal proliferation with development of a coarctation like stenosis He also points out that, in accordance with Bernoulli's principle the fall in pressure at a point of constriction may well tend to potentiate or increase the narrowing These changes, however, probably require a more marked and abrupt reduction in cross sectional area than would ever be accepted as a satisfactory anastomotic procedure. It is almost an invariable finding that the lumen, through a coarctation of sufficient significance to be diagnosed clinically, is minute. Thus, if a large number of collaterals are not sacrificed (and collateral arteries, usually intercostals, should not be needlessly sacrificed in accomplishing the operative procedure), the patient should benefit significantly by any increase in diameter that can be achieved.

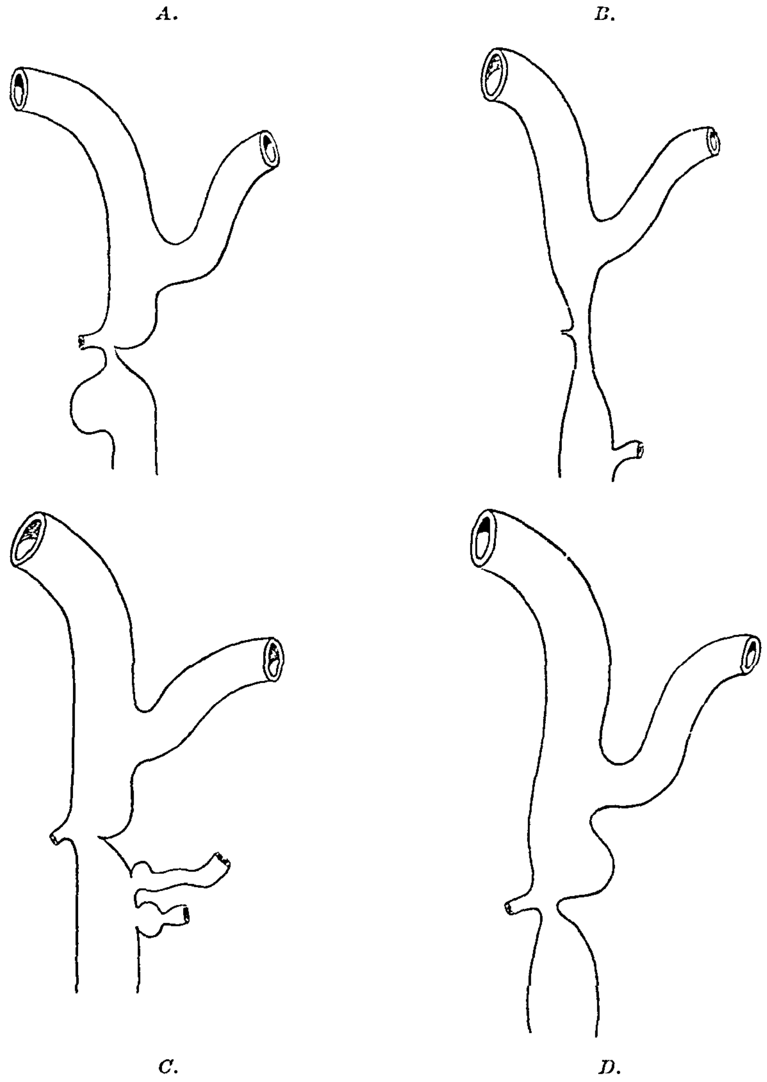

Fig. 10.—Examples of types of coarctation where grafting procedures are frequently indicated. Occasionally the orifices of aneurysmal intercostal vessels, as depicted in *C*, may be carefully purse-string sutured and the involved aortic segment thus preserved. An example of a coarctation similar to *B* is discussed at some length in the text. We would not use a graft in this instance if sufficient narrowed aorta could be resected so that a lumen diameter of 1 cm. could be accomplished.

Gupta and Wiggers,[15] in acute dog experiments, found that a reduction of more than 45 to 55 per cent in aortic cross-sectional area is required before the pressure in the proximal aorta or femoral artery is affected. This corresponds to a reduction in diameter of one fourth to one third. They also found that total peripheral resistance was not significantly raised until the constriction approximated 70 per cent of the natural aortic diameter. Similarly, Clatworthy and associates[16] found in the dog "little influence on the passage of blood through a stenotic area until that area is reduced to at least 25 per cent of the normal cross-sectional area or about 50 per cent of the normal intraluminal diameter."

A person with coarctation has already made excellent physiologic and anatomic adjustment to much more severe obstruction than that of these experimental conditions, and should thus have normal findings with even greater deformity than obtained in the experimental situations, which is certainly greater than would be acceptable as an operative result. (See the appendix for an elementary mathematical analysis of this problem.)

Data will be presented suggesting that moderate residual constriction is well tolerated by the patient.

In several infants with extremely small aortic segments in the vicinity of coarctation it was tempting to use a graft to enlarge a soda-straw lumen and to overcome the theoretical objection that, in accordance with Bernoulli's principle, these segments may not grow. However, this latter point is not now definitely settled and certainly the use of a static nongrowing graft in an infantile aorta is out of the question. In adults or in large children, with one exception, we have always been able to accomplish an anastomosis, the internal diameter of which approximated at least 1 cm. This is indeed as large as the lumen of many of the hypoplastic aortas and in all cases has given what seems to be a satisfactory operative result without significant residual pressure gradient. An occasional patient has had residual hypertension and we have tried to evaluate the possibility of residual coarctation as an etiologic factor.

5. *Residual Hypertension.*—In the course of postoperative follow-up studies of our patients treated for coarctation of the aorta, it has become apparent that as a group they tend to have extremely labile blood pressures; a reason for this will be suggested. But, in addition to having labile blood pressures, approximately 10 per cent of the patients on repeated follow-up visits remained consistently hypertensive. With the assistance of our Division of Research and Cardiovascular Laboratory,* we have hospitalized 4 of these patients for study, including direct pressure measurements and contrast-medium visualization of the aortas. To throw additional light on this problem, we also have been fortunate in having the opportunity to restudy the 1 patient, mentioned previously, in whom an anastomosis of definitely less than 1 cm. in diameter was accomplished.

She was a 12-year-old child (M. D.), who was asymptomatic, but had typical coarctation findings with blood pressures in the arms of 160/85 to 165/85 mm. Hg. Pressures were not obtainable in the legs. The surgical problem and solution as diagrammatically drawn in the patient's chart postoperatively by a member of the house staff are shown in Fig. 11. The reasoning at the time was that, although homografts were readily available, this child's aorta was not completely full grown and the graft might become a point of relative coarctation. More important was concern as to the long-term fate of a homograft placed in a 12-year-old child. *This girl has now been observed for* 4 years and representative blood pressure readings are shown in the accompanying graph (Fig. 12). Clinically she has remained asymptomatic, although, to palpation, pulses in the lower extremities are not as forceful as

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*We are indebted to Dr. Harriet P Dustan, Dr F Mason Sones, Jr., Dr Earl K Shirey, and Mr Frederick Olmsted for their assistance

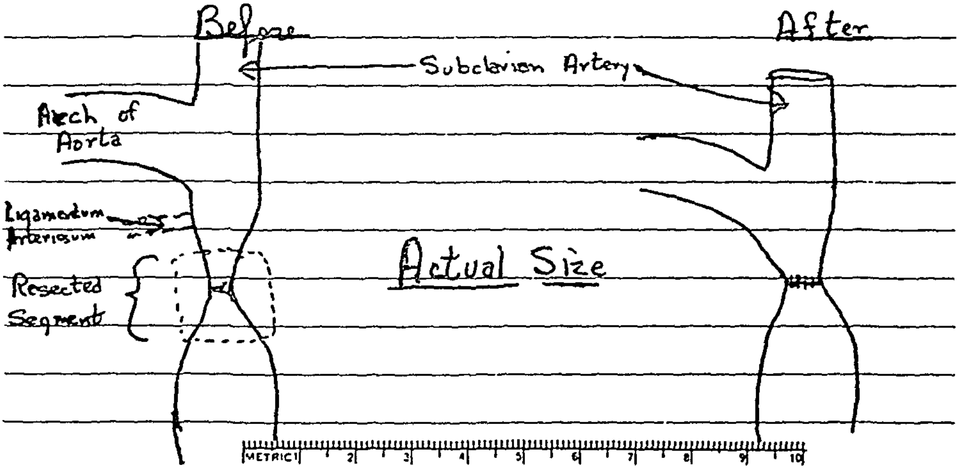


Fig. 11.—Drawing from the chart of Patient M. D. Note that the artist stated the drawing to be actual size and a scale has been affixed so that the reproduced size may be estimated.

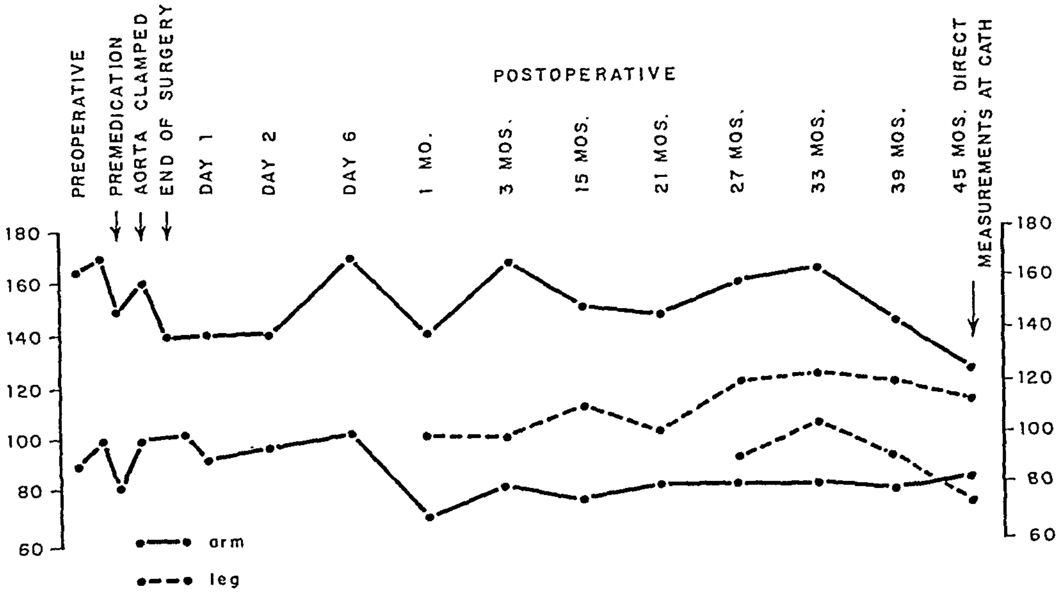
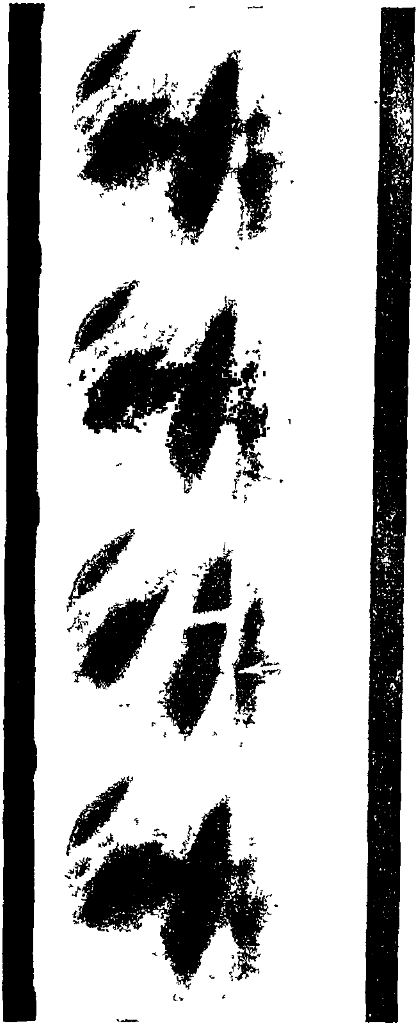


Fig. 12.—Blood pressure observations over almost 4 years on Patient M. D. The decrease in pressure gradients between the arms and legs suggests some aortic growth in the vicinity of the anastomosis. In view of the hypoplasia in her aortic arch system, the residual minor hypertension is probably due to a small central reservoir.



[illegible] 4 frames of 16 mm motion-picture film which shows injection
of [illegible] ortic arch of Patient M D, 4 years after surgery *The next*
to [illegible] retouched to increase the contrast The catheter tip can be
see[illegible] *on the left Note the small caliber of the transverse aortic*
arc[illegible] ll as the hourglass deformity (*arrow*) of the anastomotic site

TABLE II. DATA ON PATIENTS STUDIED WITH RESIDUAL HYPERTENSION

PT.	AGE	SEX	PREOP. B.P.		OPERATIVE FINDINGS	POSTOP. INTERVAL (YR.)	POSTOP. B.P. ARMS	DIRECT B.P. UNDER SEDATION		COMMENT
			ARM	LEG				ABOVE	BELOW	
M. D.*	12	F	165/90	0	Long tapering coarctation	4	140-150/80	122/74	112/72	Small anastomosis (<1 cm.); result gratifying; diminished femoral pulses
H. H.	12	M	180/100	130/?	Total coarctation, vicinity of coarctation hypoplastic	3½	160/80-180/86	152/92	142/90	1.5 cm. area of 50 per cent narrowing; strong femoral pulses, persistent tachycardia; B.P. falls with rate
W. H.	27	M	220/110	0	Hypoplasia of proximal aorta	4	150-180/90	175/100	176/110	No narrowing; strong femoral pulses; small aortic arch; very rapid flow
E. A.	29	M	210/106	130/120	Typical; no hypoplasia	2	110/60-180/100	118/68	104/72	Mild A.I.; minimal narrowing at anastomosis; excellent femoral pulses
R. T.	30	M	240/90	130/110	Typical; lower thoracic aorta small	3	186/72-190/80	146/85 L. vent.	144/82 180/15	A.S., A.I.; anastomosis 60 per cent width of arch; full femoral pulses

*Patient M. D., who has already been discussed, is the individual with the relatively small anastomosis.

those above The proximal aorta was catheterized via the right brachial artery and contrast studies as well as pressure measurements were made Pressure in the proximal aorta was 122/74 mm Hg, while that in the femoral artery was 112/72 mm Hg The motion pictures show definite evidence of residual narrowing but, in comparison to the small caliber of the transverse aortic arch this narrowing seems minor and the contrast medium passes this area with high velocity and no suggestion of delay (Fig 13) It had been contemplated that this girl would require reoperation with grafting in her adult life In view of these studies, it seems doubtful to us that the improvement to be obtained would be worth the risk entailed At the present time (Fig 12), this patient, in spite of her small anastomosis, is not significantly hypertensive These findings suggested to us that residual narrowing at the site of anastomosis was probably not a major factor in the pathogenesis of persistent hypertension

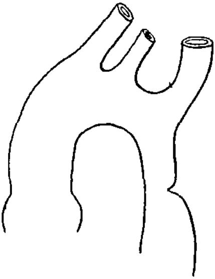


Fig 14—Tracing of an enlargement from a 3 mm motion picture frame on Patient F A aged 29 years 2 years following surgery This patient has excellent femoral pulses and a pressure gradient under direct measurement was 14 mm of mercury systolic This patient also has mild aortic insufficiency

As mentioned, 4 other patients were studied in this regard Their data are summarized in Table II In spite of the residual hypertension, all of these patients had excellent femoral pulsations on examination and, under essentially basal conditions with sedation, directly measured gradients across the area of coarctation are small, the maximum being 14 mm of mercury systolic pressure In 2 patients there was significant detectable residual narrowing One of these at the time of operation had very definite hypoplasia in the immediate vicinity of the coarctation which undoubtedly accounts for this finding The other one does have some residual deformity at the anastomotic area (Fig 14)

In 2 patients contrast medium was seen to regurgitate across the aortic valve in diastole confirming the presence of mild aortic insufficiency which undoubtedly contributes to their systolic hypertension

In 3 of the 4 patients, at the time of surgery the small caliber of various portions of the aorta was noted This finding was also noted by individuals doing the recheck contrast medium studies

The team that studied these patients was also most impressed by the high velocity of flow in the aorta. This is readily demonstrable with the motion pictures obtained using the photofluorographic unit and image intensifier. The finding of relatively small aortas and high velocity flow suggests that a large component of the hypertension in these patients is related to a small inelastic central arterial reservoir, so that the hypertension is not unlike that seen in the arteriosclerotic person, that is, chiefly a systolic hypertension with a relatively normal diastolic pressure. It is likely that there is deficient or abnormal elastic tissue in many of these aortas. However, we do not have sufficient histopathologic proof of this at the present time to warrant further discussion. If patients with coarctation are considered frequently to have a small central arterial volume and decreased vascular elasticity, their blood pressure might be expected to vary roughly in proportion to variations in heart rate. The thought is ingrained in these patients that their well-being is closely allied to low blood pressure; hence, the mere application of the blood pressure cuff provokes an emotional stimulus that may result in tachycardia. Thus, it is not surprising to get widely varying and frequently hypertensive readings in postcoarctation patients. Of the 4 hypertensive patients discussed here, 2 are hyperkinetic and, at almost every examination, have had rather marked tachycardia. In both, blood pressure has responded rather dramatically to Rauwolfia preparations that have also slowed the heart rates.

The 4 patients restudied for hypertension are male; we do not have a clear-cut example of this postoperative problem in female patients. This suggests that the male propensity for arteriosclerosis may be accelerated by coarctation. In this limited series, the age of the patient seems to have little bearing on the persistence of hypertension.

We do not propose here to settle the dispute concerning the pathogenesis of hypertension in coarctation of the aorta. There are proponents of simple mechanical obstruction, and also of renal ischemia.[17] We suggest that postoperative residual hypertension may be largely explained on the basis of the structural characteristics of the blood vessels, and that comparable factors must certainly be applicable preoperatively. In the course of re-evaluating the postoperative conditions of the 5 patients who have been discussed, it was believed to be worth while to study their renal function rather closely. It was suggested that perhaps such a patient might have a second coarctation-like lesion involving the renal circulation to maintain his hypertension. Also, if these patients had typical essential hypertension, it should be manifested in the renal circulation. Mere observation of the patients under hospital conditions was enlightening. It was apparent that this was a systolic and not a diastolic hypertension, as are both essential and renal hypertension. Furthermore, under hospital conditions, all 5 patients became essentially normotensive, which should not happen to a person having essential or renal hypertension without specific treatment. The renal function tests on these patients are summarized in Fig. 15 and Table III. Renal plasma flow and glomerular filtration rate was normal or elevated when compared to average normal values.[18] Filtration fraction was normal and total renal vascular resistance was normal or slightly decreased. Thus, none of these patients evidenced the renal vasoconstriction characteristic of essential hypertension Our results are in accord with those which Kirkendall and associates[10] found prior to the surgical repair of aortic coarctation. Such findings suggest that the hypertension of coarctation is not of humoral origin.

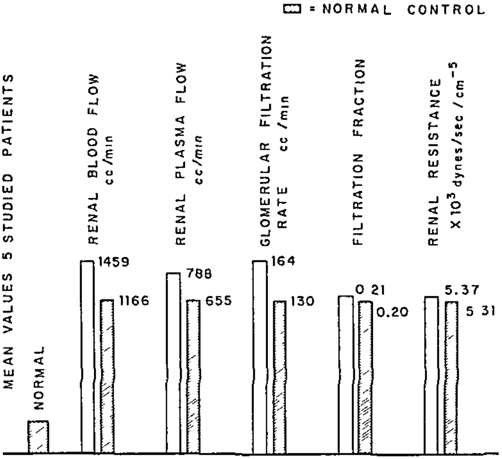


Fig 15 —Graphic demonstration of mean renal function values in 5 postoperative patients tabulated in Table III There is no evidence of renal vasoconstriction in these postoperative patients

TABLE III. TABULAR SUMMARY OF RENAL FUNCTION STUDIES IN 5 POSTOPERATIVE PATIENTS WITH MEAN VALUES AND COMPARABLE NORMAL VALUES[18]

NAME	RBF	RPF	GFR	FF	PM	R
E. A.	1,640	902	208	0.23	100	4.37
M. D.	1,877	1,070	164	0.15	107	4.11
H. H.	1,113	612	133	0.22	100	6.42
W. H.	1,366	683	186	0.27	120	6.39
R. T.	1,295	675	129	0.19	101	5.58
Means	1,459	788	164	0.21	106	5.37
Normal[18]	1,166	655	130	0.20	100	5.31

RBF = renal blood flow in c c per min , RPF = renal plasma flow in c c per min GFR = glomerular filtration rate in c c per min , FF = filtration fraction, PM = mean arterial pressure in mm of mercury, and R = renal resistance in 10^3 dynes/sec/cm^{-5}

Note that in every instance the values fall within the normal range and that the mean values exceed normal

We suggest that coarctation of the aorta as a congenital anomaly consists of not only the narrowed segment, but also of other integral defects of the aortic arch system. These defects are hypoplasia of varied caliber and extent, and deficiencies of the inherent aortic elasticity. Admittedly, this latter defect is largely hypothetical, but more than premature development of arteriosclerotic rigidity is probably present in the young persons studied. The narrowed segment only can be coped with surgically, and other factors cause residual hypertension. They are probably also major factors in the preoperative hypertension.

SUMMARY AND CONCLUSIONS

The purpose of this paper has been to discuss problems that have continued to perplex the authors in the course of their surgical experience with coarctation of the aorta in 60 patients. There are other aspects of the problems that could have been discussed, but those cited have seemed to be the major ones in that they recur with significant regularity. A discussion of this type does not warrant many firm conclusions and the primary mission when this project was initially undertaken was to clarify, rather than solve, the problems under discussion. However, the clinical research involved in assembling these data has led to the following tentative conclusions.

1. An aggressive surgical approach to the infant patient in congestive heart failure with coarctation of the aorta is indicated. In a majority of these patients, the coarctation is only a part of a complex cardiac anomaly; however, the coarctation and the frequently associated patent ductus are the most accessible parts of such problems from the surgical standpoint and operation has resulted in very gratifying results. Residual aortic hypoplasia seems to be well tolerated.

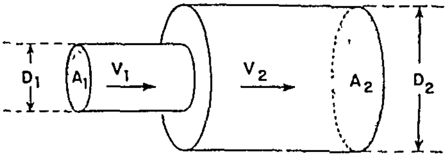


Fig. 16.—See text.

2. No conclusions can be drawn about surgical treatment of coarctations in patients more than 45 years of age. The surgical risk is certainly high, but each case must be weighed on its individual merits.

3. Experience with the postcoarctation abdominal pain syndrome is very limited. It is our impression that this complication is probably associated with extremely complete correction of coarctation and maximal increase in visceral circulation. We hope that additional reports of treatment with antihypertensive drugs will be forthcoming.

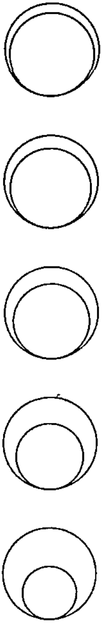
4. We believe that a strong case can be made for satisfaction with moderate residual anastomotic narrowing. It seems reasonable to avoid the use of grafts if an anastomotic lumen of 1 cm. in diameter can be accomplished without their use.

5. Postoperatively, these patients tend to have a labile blood pressure and it is thus difficult to ascertain which patients are truly hypertensive; in this series, the figure approximates 10 per cent. Study of such patients suggests

that the hypertension is due to a small inelastic central arterial reservoir rather than residual obstruction and further suggests that, in all probability the same factors play a role in the hypertension of the untreated patient

APPENDIX

It is of interest to consider the hydraulic aspect of fluid passing through a constriction This has been worked out mathematically for the flow of homogeneous fluids through rigid tube systems The problem becomes much more complicated when one considers a corpuscular fluid, such as blood, flowing through elastic vessels in a pulsatile manner



Area $\frac{A_2}{A_1}$	Diameter $\approx \frac{\sqrt{A_2}}{\sqrt{A_1}}$	if V_2 = 6 ft/sec V_1 =	Head Loss (H_L)
$\frac{5}{4}$	$\frac{2.4}{2}$	7.5	1.25 mm Hg
$\frac{4}{3}$	$\frac{2}{1.73}$	8	2.5 mm Hg
$\frac{3}{2}$	$\frac{1.73}{1.41}$	9	7 mm Hg
$\frac{2}{1}$	$\frac{1.41}{1}$	12	50 mm Hg
$\frac{3}{1}$	$\frac{1.73}{1}$	18	480 mm Hg

Fig 17 — Head loss associated with constrictions of varying magnitude The circles correspond to the area and diameter ratios given

The discussion which follows is thus obviously a gross oversimplification of the problem *as it applies to a steady flow of water in a rigid tube system*

There is very little energy loss in a closed system from fluid entering a sudden constriction The loss is associated with the exit from this constriction where there is a sudden loss of velocity and much energy is lost from turbulence (Fig 16) This "head loss" may be expressed mathematically by the following equation

$$H_L = \frac{V_1^2}{2g}\left[\frac{A_2}{A_1} - 1\right]^2 \frac{d}{114}$$

In this equation H_L = "head loss" in pounds per square inch; V = velocity in ft./sec.; g = the acceleration constant of gravity (32 ft. per sec.^{2}); and d = density of water (62 pounds per cu. ft.).

To assist in solving this equation and further to simplify grossly the problem, several assumptions are made.

V_2 is arbitrarily assumed to be 200 cm. per second which equals approximately 6 ft. per second (a not unreasonable value at the aortic valve).

1 lb. per sq. inch approximates 50 mm. of mercury; therefore a pressure of 150 mm. of mercury approximates 3 lb. per sq. inch.

V_1 is related to V_2 by the following equation:

$$V_1 = V_2 \frac{A_2}{A_1}.$$

Keeping V_2 a constant (6 ft. per second) and canceling out the density of water (62 lb. per cu. ft.) against 2 g (64 ft. per second^2) as equal to essentially unity, the equation is now solved for several common ratios of cross-sectional areas for A_2 and A_1 (Fig. 17). Note that the "head loss" is not great until the area ratios acquire an almost 2 to 1 discrepancy. It is of interest that this rough mathematical analogy is in essential agreement with the findings on a clinical and laboratory basis in vivo.

We are indebted to Mr. Frederick Olmsted, Research Division, The Cleveland Clinic Foundation, and Professor Ray Bolz, Department of Mechanical Engineering, Case Institute of Technology, Cleveland, Ohio, for assistance in this mathematical analysis.

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Discussion

(Papers by Burford [page 47] and Groves [page 60] and their Associates)

DR JOHN C JONES, Los Angeles, Calif —I would like to say that I thoroughly agree with all Dr Ferguson, Dr Groves, and their respective coauthors have said

[Slide] I would like to discuss some of the results on our patients in our experience over the last 12 years My associates and I have operated on 230 patients up until January 1 of this year

You will note that there were two deaths in the 14 patients under the age of 1, and 10 of those 14 patients were 10 weeks or younger, and the two deaths were in infants 4 and 5 weeks of age

This is a miserable group Nevertheless, I think it is worth while doing everything that can be done We don't advocate that these patients be catheterized because they are usually in failure and are very sick children

The vast majority of the patients that we have operated upon were between the ages of 6 and 30 years Eight of the patients were between the ages of 41 and 49 years and there was no mortality in the older group Two of them were 49 years of age, and all of them have done well following surgery There were 2 patients in this group who were severely incapacitated before we operated on them, and they were completely rehabilitated later after their operation

Fifteen of the last 100 patients, or 15 per cent of the last 100 patients on whom we have operated, have received homograft implants following resection of the coarctation Before we had grafts available to us we did 11 subclavian-aortic anastomoses with what we thought were very satisfactory results In these two categories we have had no deaths and no particular morbidity

Included in the mortality of 3 9 per cent of these 230 patients were 3 patients who developed mycotic aneurysms at the site of the anastomosis In other words, 33 per cent of the mortality has been due to mycotic aneurysm at the site of anastomosis Two of these have occurred in the last 6 months and the other one was several years ago

These 2 that we had recently were boys, ages 16 and 6 They occurred after a long period of no mortality Neither had pleural or wound infections and the source of their infection is not known The 16 year old boy had acne, he returned to the hospital after having been discharged from the hospital on his eighth postoperative day in what we thought was satisfactory condition When he came back he had fever and x-ray study revealed an aneurysm, he did not respond at all to intensive therapy, and he died of rupture of a mycotic aneurysm His blood cultures were positive for staphylococcus The 6 year old boy operated on 2 months later returned to the hospital after having been discharged on the seventh postoperative day His mycotic aneurysm *did not respond to intensive chemotherapy and it* ruptured Blood cultures were negative Now in retrospect, this young boy had a history of frequent respiratory infections, having been off and on antibiotics for 6 months prior to the surgery This experience would indicate that these patients should be free of all infections without antibiotic therapy for at least 6 weeks before any cardiovascular surgery is undertaken. I believe the increasing incidence of resistant infections and remote resistant infections harbored by these patients is going to lead to more frequent complications of this sort, and this is a complication that is most difficult to deal with.

You will note that we have not carried out the subclavian aortic anastomosis since we have had grafts available, but nevertheless we have felt that these results over a long-term period have been quite satisfactory.

[Slide] Recently we had a patient with a subclavian aortic anastomosis return because she was having dizziness, and it afforded us an opportunity to do a retrograde catheterization via the femoral artery. Unfortunately the dye study is not good, but in the roentgenogram itself it can be seen that at the anastomosis there is quite satisfactory lumen in spite of the fact that this girl had a hypoplastic transverse arch at the time of her surgery. She still has some residual hypertension; but nevertheless the mean pressure readings at the time of her aortograms was 110 mm. Hg, both above and below the anastomosis. It was decided by the cardiologist before we did this that her dizziness was on the basis of hyperventilation.

DR. A. G. BROM, Leiden, The Netherlands.—I am very grateful to you for giving me the opportunity to attend this meeting and to listen to so many interesting papers. I especially want to congratulate Dr. Groves and Dr. Ferguson for their investigation. I should like to make two remarks about the problem of coarctation.

First of all, upon the size of the anastomosis. [Slide] On this slide, you see on the ordinate, the quotient between the systolic pressure in the femoral and brachial artery, taken intra-arterially. So, point 1.00 means that the systolic pressure is the same in both arteries. At point 1.10 the pressure in the femoral artery is higher while at 0.070 it is lower, etc. I want to emphasize that these findings are relative and have nothing to do with the absolute value of the pressure readings.

On the abscissa is shown the quotient between the surface of the anastomosis and the aortic arch as calculated, approximately, during the operation. At point 1.00 the surface is the same. At 1.10 it is more, etc. As should be expected from earlier investigations, there is only a slight difference in systolic pressure between the brachial and femoral artery as long as the anastomosis is more than 50 per cent of the aortic arch. More interesting, however, is the finding that in patients in whom the surface of the anastomosis is larger than the surface of the aortic arch, the systolic pressure in the femoral artery might be lower than in the brachial. After finding this, we went over our pictures made during the operation and then got the impression that the result of an operation for coarctation doesn't always depend upon the absolute size of the anastomosis, but also on the form of the reconstructed descending aorta. If the size is more than 4 cm. in circumference, which means about 1.3 cm. in diameter, then we think this will be sufficient in an adult.

[Slide] But, there should not be any residual waistline in the aorta; the reconstruction of the arch and descending aorta should be so that the medioventral side of the aorta becomes a smooth curve, and the nearly always present bulging of the aorta on the dorsal side should disappear. To accomplish this, we either resect more or make an incision in the bulging part. The use of hypotensive drugs and an approximator helped us to get this shape of the aorta and, at the same time, to obtain an anastomosis with a circumference of 4 cm.

I don't want to say that my fish is bigger than Dr. Jones's fish! But, we operated upon more than 300 patients and by following the above-described technique, we used only thirteen grafts.

Now, I want to say something about the histology of the coarctation. At our University, Dr. Wielenga has made serial sections of the resected specimens and he has found that there is a close relation between the ductus arteriosus and the coarctation, regardless if the ductus is patent or not. There is marked difference between the collagen-rich, elastin-poor, fibrous tissue of the ligament and the elastic tissue of the aorta. The extension of this ductus tissue is pretty much the same in all investigated specimens. It goes from the point of insertion around the whole of the stenotic aorta On the ventral side, and at the point of *insertion of the ductus into the aorta, it makes up for the whole of the media* of the aorta and on the lateral and dorsal walls it is between the intima and the media

[Slide] Right here is the insertion of the ductus and you see this typical, elastin poor, fibrous ductus tissue making up the whole of the media of the aorta, and on the opposite side you will find that the same tissue is present between the media and the intima of the aorta Dr Wielenga could locate this fibrous ductus tissue in many serial sections and it followed always the same pattern—from the place of insertion, inside the media, at the site of the stenosis, around the aortic wall, regardless if the ductus was patent or not This ductus tissue has also been found in normal aortas, but there it is limited only to the place of insertion of the ligament

Thank you once again for the privilege of entering into this discussion I apologize to the members of the Society for taking more than 3 minutes of their time, but the subject of coarctation of the aorta is not only near to the heart of the patient, but also very close to my own

DR GEORGE H. HUMPHREYS, New York, N Y.—I, too, appreciated very much these two papers, and hesitate, after the large series of Dr Jones and Dr. Brom, to bring the results of our smaller series to you, but I feel that this is a good chance, as Dr. Groves brought out, to compare notes

Since 1947, when we started doing coarctations at the Presbyterian Hospital in New York, we have had 86 cases Our results have been remarkably similar to those reported, with one exception We have not found many in the infantile group, in spite of the fact that, since publication of the first report from St Louis, our pediatricians have been very much aware of this situation and have been looking for such patients

We have, as a matter of fact, operated upon only 3 infants less than 3 years old There were no deaths in this group, but 1 of these patients did have a recurrence of his coarctation 5 years later.

I would like to ask whether either Dr Ferguson or Dr. Groves has seen any recurrent coarctation in any of their cases done in infancy

We were aware, of course, of the growth factor. These operations were done with interrupted sutures of fine catgut in the hope that growth would not be interfered with The patient whose coarctation recurred was operated on again successfully and is doing well Incidentally, none of these patients had any other lesions

In regard to the older age group, like the series from Cleveland we have had 3, 2 aged 47 and one aged 45 One of these was corrected with a bypass graft and the other 2 were done by direct anastomoses One of the patients died of coronary occlusion 6 weeks after successful recovery from operation

This brings up the question as to whether reduction of hypertension in the proximal aortic arch in a patient with arterial disease is really a good idea or not

Like Dr. Jones, in the early period we resorted to subclavian turndown [Slide] We have here a postoperative angiocardiogram of a patient who had such an operation done approximately 2 years before this picture was made This shows that the subclavian remained small, the anastomosis is approximately only 1 cm in diameter This patient was an adolescent girl and later became a professional tamer of wild horses She had no difficulty whatever physiologically.

We have done 11 subclavian turndowns Most of the patients do have some residual hypertension. We have done, since this operation became obsolete, 12 grafts, and many of these patients also have some hypertension remaining

[Slide] This is a study done on a patient with a graft who did have some residual hypertension; as you see, 168/64 mm Hg after operation, with a differential of 125/55 in the femoral artery This patient had a homograft which became calcified, and I believe this lends support to the concept that it is not a reduction in lumen size but perhaps the rigidity of the wall in the intervening vessel which may play some part in the residual hypertension, since so far as we know the lumen was not compromised in this patient at all

It also shows that, whereas, before operation there was a lag period in time between the brachial and the femoral simultaneous pressure readings, after operation this lag was eliminated and physiologically this patient is in good shape.

[Slide] The final slide will illustrate the slow return of patients to full recovery. This is as measured by ballistocardiogram, which we feel gives a good indication of the mechanics of recovery from coarctation. The K wave here is not present in the preoperative coarctation. It appears immediately postoperatively in a small form, but gradually gets bigger, and not until 1 year later is it of approximately equal size to the I wave, which is the normal situation, so that, even though the anatomy is restored essentially to normal immediately, there is a rather long, slow recovery period.

There are many other areas in which I would like to compare notes, but time does not permit. Our over-all mortality was approximately 5 per cent, 3 patients dying in the early period of problems which I think would no longer bother us; one immediate death when the clamps were removed, one of hemorrhage due to an inadequately tied intercostal, and one of overtransfusion.

Two late deaths have occurred, one of coronary occlusion as I have already mentioned, and one of mycotic aneurysm similar to those Dr. Jones described.

DR. NATHAN K. JENSEN, Minneapolis, Minn.—The discussions by Drs. Jones and Brom and Dr. Humphreys have been timely.

I wish to record a brief case report dealing with repair of coarctation in the over-45 age group. I think Dr. Humphreys' remarks were very good in this respect. If the individual has advanced generalized arteriosclerotic disease, the reduction of the hypertension may present a hazard. However, if the individual does not have evidence of generalized arteriolar sclerosis, then we feel that it is safe to reduce the hypertension by excision of the coarctation.

This was well illustrated by one of our patients who confessed to 58 years of age. Her husband thought she was 50. She had successfully perpetrated this little deception for 30 years. This woman was known to have severe hypertension for at least 10 years prior to her referral for surgery. Her blood pressure during that time ranged from 230/100 to 250/120 mm. Hg. Physical examination revealed no evidence of generalized arteriolar sclerosis. The eye grounds were normal, and the electrocardiographic studies showed only left ventricular preponderance. There was no evidence of cerebral damage.

Surgery revealed an uncalcified tough vessel free of atheroma and easy to work with. Correction of the coarctation was readily accomplished. The patient's blood pressure was normal immediately after surgery and is now, 3 years later. She remains well and has had no sequelae.

DR. EGBERT H. FELL, Chicago, Ill.—The Society has been greatly privileged to hear these two papers, and I was particularly pleased to hear Dr. Ferguson and associates make a differentiation between coarctations of the preductal and the postductal types occurring in infancy. We agree with their report.

The preductal group, we believe, should be cared for in infancy. Our experience is limited and sad. No patient in the postductal group, diagnosed during infancy, to date has required surgery. We have had one death; an infant died of heart failure within 24 hours of admission to the hospital.

Dr. Gasul and his associates have diagnosed and watched a good number of these patients and have kept them well above the age of 3 to 6 years without a mortality.

[Slide] A few slides will, I believe, confirm and contribute to Drs. Groves and Effler's paper. This drawing was made at surgery 12½ years ago. There is a 4 cm. long stenotic area at the isthmus and a stenosis of the subclavian artery at its origin. The patient is now 25 years old and living a normal life. At surgery, mobilization of the aorta was accomplished without injury to the collaterals and the resulting end-to-end anastomosis was about two thirds the size of the proximal lumen of the aorta. The blood pressures in the right arm and legs are equal, that in the left arm, obviously, remains lower. This patient was operated upon before aortic grafts were used. I believe this long term result should encourage us to attempt more direct end to end anastomoses and less grafting in young individuals

[Slide] This slide shows a coarctation occurring in a 21 year old woman with a golf ball sized aneurysm just distal to the coarctation, and a slightly smaller aneurysm of the second intercostal artery near the apex of the left chest cavity. At surgery, 3 years ago, the aneurysms and coarctation were resected and excellent approximation and end to end anastomosis were accomplished without the use of a graft. This lady since has had a child and is living normally

[Slide] This drawing shows a 10 cm long coarctation in a 16 year old boy We believed at first a graft would be required, but behind this large subclavian artery in the apex of the left chest cavity was this tortuous aorta The left common carotid was proximal and the tortuous portion ended at the subclavian artery The aorta was divided at the junction with the subclavian and the tortuous portion brought out from behind the vagus and recurrent nerves The 10 cm hiatus was easily bridged. The patient had a satisfactory postoperative course

[Slide] This slide shows the pathology of one of the 2 patients who required a graft This long coarctation beginning just above the diaphragm to below the renal arteries was left in place and a homograft was used to bypass it, using and end to side anastomosis at both levels The preoperative blood pressure in the upper extremities was 260/130 and postoperatively it continued high to 200 mm. Hg systolic and about 260 mm Hg in the lower extremities (a gain of 160 mm). Much time was spent studying this patient's kidney function *and there was some diminished kidney function on the left side Exploration of the* vessels of the kidneys showed minute blood vessels going to the left kidney and normal vessels on the right The left kidney was removed, following which the blood pressure came down to 170/95 mm Hg Just before leaving Chicago, I learned that this boy was recovering from a cerebral accident

[Slide] This aortogram shows another very difficult and rare coarctation. This, we believe, is an acquired coarctation Starting just distal to the left subclavian artery, the aorta was hard, nodular, and stenotic The aortogram shows a narrowed, irregular lumen to the iliac arteries We explored this woman 5 years ago, hoping that we might be of help to her We could do nothing Two months ago she was seen and was free of most of her coronary pain, but continued with severe hypertension, and no blood pressures were obtainable in the legs or the right arm She may have "pulseless disease" Time does not permit further discussion of this unusual problem

DR GEORGE H A CLOWES, JR, Cleveland, Ohio—I hesitate to bring an even smaller series before the Society, except that we have had an experience that might be of interest to others

About 8 years ago we were asked to deal with a boy who was then 8 years old He had a long coarctation with a hypoplastic left arch and a hypoplastic left subclavian artery We had no graft available to us, and felt that we would like to do something

A clamp was placed on the left common carotid artery We waited 20 minutes and nothing happened The anesthetist assured me he could feel a pulse in the left carotid Obviously the collateral circulation was quite good We divided the carotid and turned it *down to make an anastomosis to the distal aorta* The boy's blood pressure slowly came back to normal and has continued to be so for the 8 years He plays football and is in every respect a perfectly normal fellow

I think that this is of importance primarily, that a piece of normally elastic vessel was put in there which perhaps is rather better than a stiff piece of homograft that might be by this time rather smaller than the normal vessel which has grown gradually in size

We did study this chap by arterial punctures above and below the anastomosis Both the pulse tracings are normal and pressures are normal

DR. FERGUSON (Closing).—One specific question was asked by Dr. Humphreys. We have had no recurrences of coarctation, but the series is yet young. The average follow-up time now is only 2 years in the 8 children.

We have a group of children, of course, in whom the diagnosis of coarctation was established during infancy, but who were not in heart failure. These children were followed until a more satisfactory time; that is, 8 or 9 years of age, and repair done then. It is interesting that no child in this group had an intracardiac shunt or an associated patent ductus.

The most illuminating thing to us about this series is the fact that if an infant comes into the hospital in heart failure and an intracardiac shunt is diagnosed, then it certainly behooves the pediatrician and the surgeon to look for an associated coarctation, because these children can be saved by prompt surgical correction of the coarctation.

DR. GROVES (Closing).—Dr. Jones, we have operated upon only 3 patients over 45. One of these died of mycotic aneurysm about a month later; one is living and well, and the other, with regard to what Dr. Humphreys said, got a beautiful reduction in blood pressure, but when he died a week later his brain was mush. He, too, could not tolerate the successful lowering of the blood pressure with his arteriosclerosis.

The longest follow-up in our infantile group is 4 years. We have not recognized the clinical recurrence of coarctation. We have several other postoperative angiocardiographic studies similar to the ones I have shown which show a residual hypoplasia comparable to what was there at the time of surgery, but we are not aware that true coarctation has recurred.

AN ANALYSIS OF DEATHS FOLLOWING CARDIAC SURGERY

James L. Harrison, M.D. (by invitation), Julio C. Davila, M.D., Bart D. Iaia, M.D. (by invitation), and Robert P. Glover, M.D., Philadelphia, Pa.*

CARDIAC SURGERY has been practiced for only a few years and has stimulated remarkable progress in diagnosis, anesthesia, and in surgical thought and technique. Through the years, new surgical methods, arbitrary classifications of cardiac disease, and indications for operative treatment have been proposed. As these and the results of their application have improved, many interpretations and conclusions based on considerable experience, but sometimes on older concepts, have made their way into the literature, nearly always emphasizing the successes. As the era of open heart surgery comes into its own, it seems advisable to review at least the most obvious failures resulting from closed heart surgery in search of explanation and clarification for what often appeared to be perplexing problems, to attempt to sift out misconceptions and errors in judgment, to define limiting physiologic and pathologic factors as they exist today, and to re-evaluate certain areas where knowledge is obviously lacking.

Table I shows the total number of thoracic operations, total hospital deaths both medical† and surgical, the number of closed heart surgical operations, and the total number of closed heart surgical hospital deaths that have occurred from December, 1952 through December, 1957, on the services of the Glover Clinic group at the Presbyterian Hospital in Philadelphia. This report is particularly

TABLE I. SUMMARY OF CASES IN THIS STUDY

	1952	1953	1954	1955	1956	1957	TOTALS
Total admissions	1	82	142	231	241	534	1,231
Total thoracic operations	1	71	98	165	188	403	926
Total hospital deaths (med. & surg.)	0	15	11	28	17	27	98
Total closed cardiac operations	1	66	76	120	126	155	544
Total closed cardiac surgical deaths	0	12	6	23	12	14	67
Per cent mortality of closed cardiac surgical deaths	0%	18%	8%	19%	10%	9%	12%

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

*Research Fellow of the American Heart Association, 1958-1959.

†Patients admitted to the cardiovascular service for study and evaluation but who were not operated upon.

concerned with 67 closed heart surgical deaths, listed consecutively without omission, which represent the entire mortality experience of this group for this type of surgery in this institution for this 5-year period.

Table II lists the 544 closed heart surgical operations and 67 deaths that occurred over the 5-year period. It will be noted that pulmonary valvotomy, closure of patent ductus arteriosus, and exploratory cardiotomy have been attended with no mortality. On the other hand, mitral commissurotomy has had a 7 per cent mortality; aortic commissurotomy, 21 per cent; mitral purse-string, 35 per cent; and miscellaneous operations, 18 per cent.

TABLE II. CLASSIFICATION OF DEATHS BY OPERATION, 1952-1957

OPERATION	NO. OPERATED CASES	DEATHS	% MORTALITY
Pulmonary valvotomy	17	0	0
P.D.A. ligation or division	19	0	0
Exploratory cardiotomy	32	0	0
Mitral commissurotomy	275	20	7
Aortic commissurotomy	57	12	21
Mitral purse-string	54	19	35
Miscellaneous*	90	16	18
Totals	544	67	12

*Resection coarctation of aorta; pericardial poudrage; pericardiectomy; infundibular resection; tricuspid commissurotomy; closure interatrial septal defect; excision left ventricular aneurysm; and Hufnagel valve insertion.

Table III is a breakdown by disease in the closed heart surgical group. In the aortic stenosis and mitral insufficiency groups, in which aortic commissurotomy or mitral purse-string operations were performed, 3 and 6 cases, respectively, had associated mitral stenosis for which mitral commissurotomy was also performed. Table IV lists the cases according to clinical classification[1,2] and sex.

TABLE III. CLASSIFICATION BY DISEASE

PRIMARY HEART DISEASE—67 CLOSED CARDIAC SURGICAL DEATHS

	NO. CASES	SUBTOTAL
Congenital		
Interatrial septal defects (2,* 1†)	5	
Coarctation of aorta	2	
Aortic stenosis	1	
Infundibular stenosis (tetralogy of Fallot)	1	
		9
Acquired		
Rheumatic heart disease		53
Mitral stenosis	20	
Aortic stenosis (3†)	11	
Mitral insufficiency (6†)	19	
Tricuspid, mitral and aortic stenosis	1	
Aortic and mitral insufficiency	1	
Myocarditis	1	
Arteriosclerotic heart disease		4
Postmyocardial infarction (angina)	3	
Left ventricular aneurysm	1	
Unknown		
Constrictive pericarditis	1	1
Grand total		67

*Anomalous pulmonary veins.

†Associated mitral stenosis.

TABLE IV DISTRIBUTION OF CASES BY CLINICAL CLASSIFICATION AND SEX

NEW YORK HEART CLASS	MALES	FEMALES	TOTALS	AM ASSOC ANES CLASS	MALES	FEMALES	TOTALS
IIC	1		1				
IIIC	2	2	4				
IIID	8	13	21	III	8	16	24
IVD	11	15	26	IV	20	23	43
IVF	6	9	15				
Totals	28	39	67		28	39	67

In Table V the cases are grouped according to type of operation and time of death in relation to surgery Operating room deaths are defined as those which occur any time during the course of anesthesia or surgery in the operating room Immediate postoperative deaths are those occurring in the first 48 hours following surgery Delayed postoperative deaths are those occurring after 48 hours but during the period of hospitalization

TABLE V GROUPING ACCORDING TO TYPE OF OPERATION AND TIME OF DEATH

OPERATION	TIME OF DEATH O R	IMMEDIATE	DELAYED	TOTALS
Mitral commissurotomy	2	4	14	20
Aortic commissurotomy	6 (2*)	4	2 (1*)	12
Mitral purse string	6	8 (3*)	5 (3*)	19
Mitral and tricuspid commissurotomy		1		1
Hufnagel valve procedure	1			1
Pericardiectomy	1			1
Pericardial poudrage		2	2	4
Closure interatrial septal defect	1	1	3 (1*)	5
Infundibular resection		1		1
Resection coarctation of aorta	1		1	2
Resection left ventricular aneurysm		1		1
Totals	18	22	27	67

*Coexisting mitral stenosis for which commissurotomy was performed

Table VI is a compilation of clinical and other features for the mitral commissurotomy, aortic commissurotomy, and mitral purse string groups which comprise 51 of the 67 deaths under discussion The other 16 cases are considered later in the text

Mitral commissurotomy refers to the standard operation as described previously,[3, 4] although 9 of the patients had anterolateral commissurotomy only

The twelve aortic commissurotomies were performed by the transventricular route as described elsewhere Of the 12 deaths under discussion, 6 of the patients were operated upon with the now obsolete three bladed dilator[6] and 6 with the two bladed Brock dilator[7] The current technique[8] was used in only 2 of the latter Circumferential suture of the mitral valve was carried out as described in previous publications[9, 10, 11]

The obviously high mortality rates in the aortic commissurotomy and mitral purse string groups are in part, related to the development of these procedures Better selection, refinement of method, and progress in management and anesthesia[12, 13] have currently reduced these to acceptable rates[8, 10, 11, 14] This study further represents the group's experience largely in acquired valvular cardiac disease. The bulk of the congenital heart surgery is performed at St. Christopher's Hospital for Children in Philadelphia and does not form a part of this survey.

DISCUSSION OF MORTALITY IN SURGERY FOR MITRAL AND AORTIC STENOSIS AND MITRAL INSUFFICIENCY

Table VI summarizes most of the information pertaining to the mitral commissurotomy, aortic commissurotomy, and mitral purse-string groups.

Patients with mitral stenosis tolerate surgery much better than those with aortic stenosis or mitral insufficiency, and the majority of those who die do so in the postoperative period of advanced disease or of induced mitral regurgitation. On the other hand, patients with aortic stenosis and mitral insufficiency are faced with a high immediate risk, related particularly to more profound myocardial and systemic changes. It is apparent from the distribution by classification,* in all categories, that nearly all the patients were in far-advanced stages of disease. This is particularly true in the aortic stenosis and mitral insufficiency groups.

The ratio of males to females who die in the mitral commissurotomy group is higher than for the over-all series.[15] In contrast, the number of males undergoing aortic commissurotomy is about three times as high, and there seems to be no relation of sex to surgical risk in this group.[8, 15] In the mitral insufficiency group, the ratio of males to females undergoing surgery is about the same as for those who die.[14, 15]

The age of the patient undergoing mitral commissurotomy may be related to the surgical risk in that the median age among the fatal cases is 4 years higher than in the over-all group of 275 cases.

The median age of patients with aortic stenosis who died was also 4 years greater than that of the over-all operative material (57 cases). The median age of the group with fatal mitral insufficiency was only 1 year greater than that of the series of 54 patients operated upon.

Although it is implied, in the figures listed, that most of the patients in all categories who died following surgery had rheumatic fever at or about age 15, it must be borne in mind that this figure depends on the patient's recollection of the onset of disease and is probably 4 to 6 years higher than it should be.[16]

It is interesting to note that cardiac symptoms were present for about one third of the total interval since onset of disease. However, frank congestive cardiac failure did not begin until the last 1½ to 3½ years prior to surgery. It

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*The Functional-Therapeutic New York Heart Association Classification[1] is as follows: Class I—no limitation of activity; Class II—slight limitation of activity; Class III—moderate to great limitation of activity; Class IV—unable to carry on any activity without discomfort. Class A—no restriction required; Class B—restriction in unusual activity; Class C—moderate restriction of ordinary activity; Class D—marked restriction of ordinary activity; Class E—should be at bed rest.

American Association Anesthesiologists Classification of physical status[2]: Class I—no organic pathology; Class II—moderate but definite systemic disturbance; Class III—severe systemic disturbance; Class IV—external systemic disorders (eminent threat to life); Classes V and VI—emergency states.

TABLE VI TABULATION OF DATA ON MITRAL COMMISSUROTOMY, AORTIC COMMISSUROTOMY AND MITRAL PURSE STRING GROUPS

	MITRAL COMMISSUROTOMY		AORTIC (3*) COMMISSUROTOMY		MITRAL (5*) PURSE STRING	
	NO	PER CENT	NO	PER CENT	NO	PER CENT
Total cases operated	275		57		54	
No of deaths and % mortality	20	7 2	12	21 1	19	35 2
No of deaths	20	100	12	100	19	100
Operating room deaths	2	10	6	50	7	37
Immediate postoperative deaths	4	20	4	33	7	37
Delayed postoperative deaths	14	70	2	17	5	26
Classification, New York Heart Association						
Class IIIC					1	5
Class IIID	10	50	2	17	5	26
Class IVD	6	30	6	50	7	37
Class IVI	4	20	4	3	6	32
Classification physical status (American Association Anesthesiologists)						
Class III	10	50	1	8	7	37
Class IV	10	50	11	92	12	63
History of rheumatic fever or related disease						
Definite	1	65	6	50	15	78
Vague	3	15	3	25	2	11
None	4	20	3	25	2	11
Sex distribution						
Males	7	5	9	75	2	11
Females	13	65	3	25	17	89
Ages (in years)						
Median	44		44		32	
Range	33 63		30 50		18 52	
Number of years rheumatic fever or cardiac disease present						
Median	10		12		6	
Range	5 42		13 42		5 36	
Number of years taking digitalis						
Median	4		2		6	
Range	0 25		0 13		1 11	
Number of years since onset of frank congestive cardiac failure						
Median	2½		1½		3½	
Range	0 10		0 13		1 18	
Congestive cardiac failure on admission						
Frank	9	45	3	25	9	47
Borderline	2	10	4	33	2	11
Not present or fully compensated	9	45	5	42	5	26
Possibility of preoperative rheumatic fever activity	4	20	2	17	6	32
Possibility of or suggested digitalis intoxication	8	40	5	42	11	58

(Cont d on next 2 pages)

TABLE VI—CONT'D

	MITRAL COMMISSUROTOMY		AORTIC (3*) COMMISSUROTOMY		MITRAL (5*) PURSE-STRING	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Electrocardiogram (preoperative)						
SR	2	10	9	75	6	32
AF	17	85	3	25	13	68
Bigeminy	1	5	(2)	(runs)		
RVH	13	65			5	26
LVH	1	5	9	75	4	21
L and RVH	4	20	3	25	4	21
Strain or overload	10	50	6	50	4	21
Partial AV block			1	8	2	11
L.B.B.B.			1	8		
Healed infarct			1	8		
Left ventricular size by x-ray (scale 0 to 4 plus)						
Median	½		3		2	
Range	0-2		2-4		1-4	
Irritable myocardium at surgery	6	30	8	67	14	74
Blood replacement at operation (c.c.)						
Median	650		1,500		1,500	
Range	500-1,500		500-2,500		500-4,000	
Thrombus in left atrium or appendage	11	55	1	8	2	11
Arterial emboli produced						
Definite	6	30	1	8		
Probable	1	5	1	8		
Postoperative shock in those surviving operation						
Immediate postoperative deaths	4 of 4		4 of 4		7 of 7	
Delayed postoperative deaths	2 of 14		2 of 2		2 of 5	
Postoperative frank CHF in those surviving surgery						
Immediate postoperative deaths	1 of 4		1 of 4		2 of 7	
Delayed postoperative deaths	13 of 14		2 of 2		5 of 5	
Mitral regurgitation						
Premitral commissurotomy	11 of 20		2 of 3			
Postmitral commissurotomy	18 of 20		3 of 3			
Increase in mitral regurgitation	17 of 20		3 of 3			
Degree mechanical correction of mitral regurgitation by mitral purse-string						
75% or more					13	68
50 to 75%					3	16
Less than 50%					3	16
Description of mitral valve (operation and autopsy)						
4-plus calcified, rigid	8					
2-plus calcified, 1-plus pliability	2					
Shoeleather with some calcification, rigid	5				2	
Shoeleather with 1-2 plus pliability	3		3 of 3		4	
Thin shoeleather 2-3 plus pliability	1				5	

TABLE VI—CONT'D

	MITRAL COMMISSUROTOMY		AORTIC (3*) COMMISSUROTOMY		MITRAL (5*) PURSE STRING	
	NO	PER CENT	NO	PER CENT	NO	PER CENT
Kid glove, 4 plus pliability	1				7	
Normal valve consistency					1	
Marked loss of valvular substance					4	
Slight to moderate loss valvular substance					10	
Degree of mitral stenosis						
0.1 to 0.2 cm²	4	20				
0.2 to 0.8 cm²	8	40				
0.8 to 1.5 cm²	4	20				
Over 1.5 cm²	4	20				
Mitral annulus (diameter in cm)						
Median					(10 of 19) 6	
Range					5-7	
Mitral orifice (diameter in cm)						
Median					(14 of 19) 4	
Range					3-6	
Aortic valve						
4 plus calcification			10	83		
3 plus calcification			2	17		
Calcification into myocardium			9	75		
Heart pathologic findings (number)	(12)		(7)		(15)	
Muscle hypertrophy	8		6		13	
Perivascular fibrosis	8		7		10	
Recent myocardial infarcts	2		1		0	
Healed myocardial infarcts	0		1		0	
Rheumatic activity	1		1		0	
Fatty change	0		1		3	
Endocardial thrombus	3		0		1	
Significant coronary atheromatosis	5		9		5	
Lung, pathologic findings (number)	(15)		(9)		(16)	
Chronic passive congestion	14		9		16	
Pulmonary fibrosis	5		0		1	
Bronchopneumonia	4		1		2	
Pulmonary edema	4		4		9	
Pulmonary infarction	2		0		2	
Liver, pathologic findings (number)	(13)		(8)		(14)	
Chronic passive congestion	9		5		11	
Cardiac cirrhosis	3				2	
Central necrosis	1				3	
Fatty change	1		4		1	

* Associated mitral stenosis requiring mitral commissurotomy

is notable that the interval of time that patients had congestive cardiac failure with aortic stenosis is considerably shorter than with either mitral stenosis or mitral insufficiency, but it is also evident that patients with mitral insufficiency had a much shorter interval during which symptoms were present. These considerations could support the view that the patient with mitral stenosis has a long course of illness with a relatively slow progression of symptoms and deterioration. Likewise, the patient with aortic stenosis has a long course of illness with relatively slow development of symptoms but with rapid deterioration after onset of congestive heart failure. The patient with mitral insufficiency has a shorter interval of rheumatic disease, with symptoms developing late in this course, followed quickly by congestive cardiac failure of a less precipitous nature than in cases of aortic stenosis.

The electrocardiographic findings in the three groups in Table VI indicate little that would not be expected in the over-all series; however, atrial fibrillation in the fatalities was more common in mitral stenosis and occurred in aortic stenosis only when there was associated mitral stenosis. Ventricular hypertrophy was overwhelmingly right in mitral stenosis, left in aortic stenosis, but about equally distributed between right, left, and combined in the group with mitral insufficiency. The presence of conduction defects in aortic stenosis and mitral insufficiency seems definitely associated with a higher operative risk.[15, 17] The presence of myocardial irritability during surgery was determined from the operative and anesthesia protocols. It was observed in over half the fatalities, occurring in two thirds and three fourths, respectively, of the aortic stenosis and mitral insufficiency groups.

The median value for blood replacement is definitely higher in the aortic commissurotomy and mitral purse-string groups than in the others.

Thrombus was present in the left atrium or appendage twice as frequently in the fatal cases as in the over-all series for mitral commissurotomy.[15, 18] The incidence of atrial thrombosis is low for the other two categories, as expected. Arterial emboli, producing cerebral infarction, were noted unequivocally in 6 instances and probably in 1 other case.* This is about seven times more frequent than is found in the over-all mitral commissurotomy series.[15, 18] There were noncerebral peripheral emboli in 3 of the cases mentioned above.

Preoperative low-grade rheumatic activity is at times very difficult to diagnose with any degree of certainty, but its presence could not be ruled out in about one third of the fatalities under discussion.

It is well recognized that digitalis leaf or its purified derivatives have toxic properties that are frequently associated with its clinical use.[19] The diagnosis of and the degree of severity of digitalis intoxication cannot often be accurately determined and its presence is therefore listed as a possibility. There was no relation between the length of time of digitalis therapy and the suggestion of toxicity during the hospital course. Of the 24 instances of possible toxicity in the three groups under discussion, atrial fibrillation was present in 15, sinus rhythm in 8, and persistent bigeminy in 1 case.

It will be noted in Table VI that about two thirds of the cases in all three groups were in frank or borderline congestive failure on admission to the hospital. The majority of the remaining patients with mitral and aortic stenosis, and all the patients with mitral insufficiency had been in frank congestive cardiac failure at some prior time. There was evidently a wide variation in the effectiveness of previous medical management.

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*One of these was from an autopsy-proved calcific embolus causing an infarct in the right internal capsule.

In this group of cases, there is a considerable range in the completeness of hemodynamic data Most of the patients with mitral and aortic stenosis, operated upon during the period of this study, were not subjected to cardiac catheterization unless there was some special diagnostic problem Since the development of safe and reliable left heart catheterization techniques, it is our policy to study all cases of aortic stenosis by this means and to attempt more frequently to estimate degrees of regurgitation coexisting with mitral stenosis [1] In the cases of mitral insufficiency, at least right heart catheterization was done in all but 1 patient undergoing surgery, and left heart catheterization in about two thirds of them[11]

TABLE VII HEMODYNAMICS—MITRAL COMMISSUROTOMY
(PREOPERATIVE CATHETERIZATION DATA AVAILABLE IN 4 OF 20 CASES)

CASE	PA	LA OR PAW	ART	CI	PAR	REMARKS
a	60/15(30)		96/22	1 6		
b	48/28(38)		92/60			
c	36/20(26)	25/15(20)	160/80	2 3	3 9	
d	80/40(57)	45/30(35)	180/116	2/4	6/9	MS MI

Operative Pressures

CASE	LA	LV	AO	CUFF PRESSURE	REMARKS
b Preop	4/12(23)	136/5	105/22	120/80	Severe aggravation of MI produced
Postop	60/0 (30)	123/15	95/40	105/80	
d Preop	38/25	108/12	108/78		MI preoperatively, aggravation by surgery
Postop	46 23	155/20			

Figures in parentheses refer to mean pressure—all pressures in mm Hg

PA—Pulmonary artery LA—left atrium PAW—pulmonary artery wedge Art—systemic artery CI—cardiac index PAR—pulmonary arteriolar resistance Ao—aorta LV—left ventricle

In 4 cases of the 20 deaths due to mitral commissurotomy there were preoperative hemodynamic studies which are shown on Table VII In 2 of these, left heart pressures were measured at surgery In these, it is worth noting that significant increases in left ventricular diastolic pressure, concomitant with elevation of left atrial pressure, decreased aortic pressure and decreased atrioventricular gradient, all of which suggest severe, acutely produced mitral insufficiency

Hemodynamic data are available in 6 of the deaths due to aortic stenosis In 3 of these, operative measurements were made (see Tables VIII—A and B) It is important to note that there was an elevated left ventricular end diastolic pressure in all of these in the absence of demonstrable aortic or mitral insufficiency Operative measurements indicate marked reduction in the systolic ventriculo aortic peak gradient with decrease in the left ventricular end diastolic and systolic pressures in 2 and decrease in the systolic but marked increase in the end diastolic in 2 This indicates the production of significant aortic insufficiency in the former and mitral insufficiency in the others

The hemodynamic data collected in the study of mitral insufficiency patients have been reviewed elsewhere[10 11] The information pertinent to this study is summarized in Table IX Fifteen of the 18 patients had pulmonary artery

TABLE VIII A. HEMODYNAMICS—AORTIC STENOSIS
(PREOPERATIVE CATHETERIZATION DATA IN 3 OF 9 CASES)

CASE	PA	LA OR PAW	LV	AO.	CI	REMARKS
a.	25/?	26/0(14)				
b.	19/2	15/0(10)				
c.	35/8	25/15(20)	200/20	100/70	2.6	

Operative Measurements

CASE	LA	LV	AO.	LV-AO. GRADIENT	REMARKS
b. Preop.	35/6.5(23)	220/13	125/50	95	
Postop.	11/3(6)	150/5	120/60	30	
c. Preop.	62/30	250/44	140/75	110	
Postop.	?	115/52	115/?	0	AI produced

All figures in parentheses refer to mean pressure—all pressures given in mm. Hg.

TABLE VIII B. HEMODYNAMICS—AORTIC STENOSIS-MITRAL STENOSIS
(PREOPERATIVE CATHETERIZATION DATA IN 2 OF 3 CASES)

CASE	PA	LA OR PAW	AO.	CI	PAR	REMARKS
a.	68/16(28)	20/15(18)	65/56	1.4	9	
b. 1953	45/22(30)	33/20(24)	125/64	2.7	1.5	
1954	32/15(22)	(15)		3.1		

Operative Measurements (1 case)

CASE	LA	LV	AO.	A-V GRADIENT	LV-AO.	REMARKS
b. After MC	44/25/(37)	160/14	125/70	23	35	
Not after AC	60/25/(47)	120/21	84/60	26	36	Severe MI

All figures in parentheses refer to mean pressure—all pressures given in mm. Hg.

PA—Pulmonary artery; LA—left atrium; PAW—pulmonary artery wedge; Art—systemic artery; CI—cardiac index; PAR—pulmonary arteriolar resistance; Ao—aorta; LV—left ventricle; LV-Ao—left ventricular aortic gradient; A-V gradient—atrial-ventricular gradient.

TABLE IX. HEMODYNAMICS—MITRAL INSUFFICIENCY DEATHS
(PREOPERATIVE CATHETERIZATION IN ALL 18 CASES)

	AVERAGE	RANGE	DISTRIBUTION		
Pulmonary Artery (mm. Hg) (18 cases)					
Mean pressure	38	22-25	Over 35 (11 cases)	25-35 (4 cases)	Less than 25 (3 cases)
Peak systolic pressure		23-92	Over 50 (11 cases)	40-50 (4 cases)	Less than 40 (3 cases)
Left Atrial or Pulmonary Arterial Wedge (12 cases)	$\frac{37}{18}$ (29)	$\frac{22\text{-}72}{7\text{-}24}$			
Cardiac Index (12 cases) (L./min./$M.^2$)	2.2	1.1 to 2.8	2 or over (9 cases)		Less than 2 (3 cases)
Operative Pressures					
Left atrium (16 cases)	$\frac{50}{19}$	$\frac{25\text{-}100}{5\text{-}60}$	Over 25 (all cases)	V wave Over 35 (12 cases)	Over 60 (5 cases)
Left ventricular end-diastolic	15	3-45	Over 20 (2 cases)	10-20 (10 cases)	Less than 10 (3 cases)

systolic pressures over 40 mm Hg, 11 of which were over 50 mm Hg In all but 3 cases there was mean left atrial or pulmonary artery wedge pressures higher than 20 mm Hg, and there was increased pulmonary arteriolar resistance in two thirds of 9 cases in which this measurement is available

The description of the mitral valves was derived from the operative and postmortem protocols The degree of mitral stenosis, the diameter of the annulus, and the size of the orifice were estimated digitally at surgery Aortic valvular calcification was appraised by external palpation as well as by the degree of resistance to the dilating instrument In all cases in which autopsy examinations were available, these estimates of calcification have been compared with the postmortem findings and have been found to be generally in agreement

In every case of mitral commissurotomy, the stenosis was relieved to some degree However, an adequate commissurotomy as previously defined[4] was performed in only 7 of the 20 fatal cases, and in none of the 3 fatalities of combined mitral and aortic stenosis was it possible to open the mitral valve adequately Advanced calcification and scarring was the limiting factor in all of these Among the 7 cases in which satisfactory commissurotomy was possible, 3 patients died in the first 48 hours with cerebral infarction Of the remaining 4, 1 had myocardial infarction, 1 had pulmonary infarction 1 had lesser cerebral embolization with a protracted course of bronchopneumonia, and 1 had progressive congestive cardiac failure

Preoperatively some mitral regurgitation was present in over half of the patients with mitral stenosis and in 2 of the 3 combined aortic and mitral stenosis fatalities After mitral commissurotomy, mitral regurgitation was present in 18 and 3 of these two groups, respectively There was definite increase in regurgitation in 17 of the former and 3 of the latter group

Aortic commissurotomy was carried out after ventricular fibrillation or cardiac arrest had occurred in 4 instances A mechanically satisfactory aortic commissurotomy was performed in 10 patients There was postcommissurotomy aortic insufficiency in 1 according to pressure tracings taken at surgery and at autopsy in 1 a tear in a cusp with production of a false passage 1 cm in diameter was noted

In the group with mitral insufficiency the degree of mechanical correction was grossly estimated by digital appreciation of anatomic change in the function of the valve leaflets, change in size, position, and character of the regurgitant jet, and by operative hemodynamic measurements[10, 11] Mitral purse string was carried out after the occurrence of ventricular fibrillation or cardiac arrest in 3 cases In the majority of the fatalities, the mechanical improvement was marked, the limiting factor in a few being the state of the valve, particularly the marked loss of valve substance, downward contraction of valve leaflets, and lack of pliability of the valves themselves It is apparent that correction or improvement of the mechanical defect is not sufficient per se, to save many patients in the advanced stage of this disease[14] Misplaced circumferential sutures one through the left atrium with subsequent infection,[13] one obstructing the posterior descending branch of the right coronary artery, and one through the base of the aorta represented avoidable technical errors

S.M.S. MEDICAL COLLEGE

The data concerning postoperative shock and congestive cardiac failure in patients surviving surgery refer to the presence of these conditions as part of the postoperative clinical picture for which active supportive treatment was necessary. It is interesting and striking that of the fatalities occurring in the immediate postoperative period all patients showed shock and about one fourth showed congestive cardiac failure. In the delayed postoperative period, shock occurred in about one third of the cases and congestive cardiac failure in 20 of 21.

The actual heart weights in the mitral stenosis and mitral insufficiency groups were about equal, while the group with aortic stenosis had distinctly heavier hearts. It is well known that concentric hypertrophy of the left ventricle is a predominant finding in aortic stenosis while in mitral insufficiency ventricular dilatation is more evident. However, when heart weight is correlated with body surface, this relationship does not hold. It is quite likely that the discrepancy is due to the fact that the vast majority of the patients with mitral stenosis and insufficiency were in advanced states of emaciation which makes the estimates of body surface misleading. Microscopic examination of the hearts showed the findings listed in Table VI. It is interesting to note that in all the cases of aortic stenosis and in one third of the other two categories, there was significant coronary artery disease.

A comparison of heart weights of those patients having cardiac asystole during surgery (Table X), with those who did not, as well as with the groups listed by operation, shows that patients who had asystole did not show significant heart size difference; however, it is noteworthy that in such cases there was a greater elevation of left ventricular end-diastolic pressure.

TABLE X. MEDIAN HEART, LIVER, AND LUNG WEIGHTS

	BODY SURFACE (M.^{2})	HEART		LUNG		LIVER	
		GM.	GM./M.^{2}	GM.	GM./M.^{2}	GM.	GM./M.^{2}
Mitral commissurotomy (13 cases)	1.50	580	398	950	585	1,500	900
Aortic commissurotomy (9 cases)	1.63	640	370	1,090	675	1,600	1,020
Mitral purse-string (18 cases)	1.54	570	410	730	534	1,600	1,090
Cardiac asystole*	1.54	591	395	952	617	1,730	1,124
No cardiac asystole†	1.56	630	404	874	549	1,480	951

*Left ventricular end-diastolic pressure 22.1 mm. Hg (median).
†Left ventricular end-diastolic pressure 17.8 mm. Hg (median).

MISCELLANEOUS DEATHS

1. *Closure of Interatrial Septal Defects* (5 deaths).—Of the 5 deaths associated with interatrial septal defects (all secundum type), 4 were after Sondergaard closures[24] and one after atrioseptopexy.[25] Two of these patients had anomalous pulmonary veins and 1 had associated mitral stenosis. One death

occurred in the operating room, 1 in the immediate postoperative period, and 3 in the delayed postoperative period. There were 3 females, aged 25, 35, and 41, and 2 males, aged 9 and 41. Four of the patients had symptoms 5 years or longer, 3 of whom were in frank congestive cardiac failure on admission. The pulmonary artery pressures were elevated in all cases, being 38/18, 50/25, 80/36, 86/30 and 100/48 mm Hg. The first 4 had left to right shunts of 4.0, 7.0, 5.0 and 3.6 L per minute, respectively, but the patient with the pulmonary artery pressure of 100/48 had a bidirectional shunt, the exact values being unavailable for this record. In this case, the pulmonary artery pressure fell to only 92/36 after closure of the defect. The pulmonary arteriolar and total pulmonary vascular resistances in the other 4 cases were 1.7 and 2.9, 2.0 and 2.9, 5.0 and 5.5, and 5.5 and 6.2 resistance units.[76] The electrocardiogram showed right ventricular hypertrophy in 3, right and left ventricular hypertrophy in 2, with right bundle branch block in 1 of these. There was suggestive evidence of digitalis sensitivity in 2 patients, an irritable myocardium at surgery in 3 patients, ventricular tachycardia and fibrillation playing a significant role in death in 3 instances (not merely as a terminal event). Blood replacement in the 4 adult patients ranged from 1,000 to 3,000 c.c. Hemorrhage from an atrial tear followed by ventricular fibrillation was responsible for the 1 operating room death. Persistent ventricular tachycardia and other arrhythmias as well as congestive cardiac failure were responsible for the 1 immediate postoperative death, the arrhythmias being present throughout the entire hospital course and at cardiac catheterization preceding surgery. Of the delayed postoperative deaths, 2 of these patients, aged 37 and 49, had associated congestive cardiac failure and died the tenth and third day, respectively, following surgery. Both had pulmonary artery pressures above 80 mm Hg systolic. One had elevated pulmonary arteriolar resistance (5.0 units) and mitral stenosis for which a satisfactory digital commissurotomy was performed through the septal defect. The other patient had the bidirectional shunt mentioned above. One postoperative death resulted from congestive cardiac failure following an avoidable technical error which resulted in insufficiency by laceration of the posterior cusp of the aortic valve, as well as creation of an aortico-right atrial fistula. In 4 autopsies, the heart weights ranged from 400 to 640 grams. All showed hypertrophy and fibrosis on microscopic examination. The combined lung weights ranged from 1,420 to 1,720 grams. The lungs showed chronic passive congestion in 4, with edema in 3, and acute congestion in 1. The patient with the bidirectional shunt, who died 10 days postoperatively, also had extensive pulmonary venous thrombosis.

2. *Pericardial Poudrage* (4 deaths).—There were 4 deaths in the patients undergoing pericardial poudrage,[77] 2 in the immediate and 2 in the delayed postoperative period. All were males, the ages being 39, 46, 47, and 57. All were Class IVD according to the classification of the New York Heart Association and Class IV by physical status. One had predominantly rheumatic myocardial insufficiency with minimal valvular disease. The other 3 patients had histories of definite myocardial infarctions, with subsequent angina pectoris

On electrocardiogram, 1 showed coronary insufficiency, another anterior wall ischemia (the autopsy showed recent and healed myocardial infarcts), and 2 showed left ventricular hypertrophy and nonspecific myocardial damage. Two were in congestive cardiac failure on admission and 2 showed an irritable myocardium at surgery.

Two patients died 7 and 16 hours postoperatively and 2 died 7 and 8 days postoperatively, all with the picture of severe acute myocardial infarction. At autopsy, 2 showed extensive coronary disease with complete occlusion of the left anterior descending artery with healing infarcts in 1 and multiple occlusions in the other.

3. *Resection of Coarctation of the Aorta* (2 deaths).—There were 2 deaths associated with coarctation of the aorta. An 18-year-old boy who died in the operating room, had been symptomatic only 3 months, but had extensive runs of ventricular tachycardia 2 days before operation. Cardiac arrest and ventricular fibrillation occurred 10 minutes after clamping the aorta. Autopsy showed a bicuspid aortic valve with both coronary arteries arising from a common ostium. The other patient, a 36-year-old woman, who had an uneventful operation, was doing well, but unexpectedly died in her sleep on the fifth postoperative day. Perusal of the nurses' notes indicates the strong but unverifiable possibility that digitoxin overdosage through nursing misinterpretation was a contributing factor.

4. *Pericardiectomy* (1 death).—This death occurred in the operating room in a 47-year-old man who died of ventricular fibrillation following hemorrhage from a tear in a tense, greatly distended pulmonary vein. This patient had had a previous attempt at a pericardiectomy and had been in congestive cardiac failure for about 18 years.

5. *Resection of Left Ventricular Aneurysm* (1 death).—This death occurred in a 47-year-old man who had developed a large ventricular aneurysm[29] following myocardial infarction. The resection was carried out without event, although extensive thrombosis was present in the aneurysm. Postoperatively, a left hemiplegia was noted and profuse bleeding occurred through the chest drainage tube. A total of 11,500 c.c. of blood was given and eventually exploration confirmed the impression that the bleeding was not from the ventriculotomy incision but part of a general hemorrhagic diathesis. At autopsy, fibrocaseous pulmonary tuberculosis, adenocarcinoma of the stomach with bone metastases, and mural thrombosis at the ventriculotomy site were present.

6. *Infundibular Resection in a Tetralogy of Fallot* (1 death).—This patient was a very sick 24-year-old woman with long-standing cyanosis and a definite diagnosis of tetralogy of Fallot with infundibular stenosis. The cardiac catheterization data showed a right ventricular pressure of 100/4, infundibular chamber pressure of 40/8, and pulmonary artery pressure of 16/8 mm. Hg. The peripheral oxygen saturation was 49 per cent. The preoperative hematocrit was 81 per cent and the hemoglobin 22.6 grams per 100 c.c. After resection of

three fragments of muscular tissue from the infundibular obstruction,[30] a supraventricular tachycardia developed followed by shock and finally death 3 hours postoperatively At autopsy, a laceration in the right coronary cusp of the aortic valve was present, in addition to cerebral edema, infarction of the liver, and arterial and venous thrombi in the lung

7 *Mitral and Tricuspid Commissurotomy* (1 death) —This death occurred in a 34 year old woman, operated upon through a right thoracotomy Both valves were indurated and calcified, and, although both were satisfactorily opened, two to three plus mitral and one plus tricuspid regurgitation was produced There was also an associated mild aortic stenosis The patient developed hypotension at the end of the operation and died 4 hours postoperatively in spite of supportive measures Postmortem examination of the heart specimen *on the Presbyterian pulse duplicator*[31] *showed the mitral and tricuspid valves* to be inoperable

8 *General Considerations* —Among 53 cases of rheumatic cardiac disease, there was a possibility of rheumatic activity in 12

Seven of 67 patients received no digitalis prior to admission but 6 of these were digitalized during the hospital course Of the 66 patients receiving digitalis or one of the purified derivatives, 27 or 41 per cent, showed evidence suggestive of digitalis toxicity

Pericardial symphysis was present in 11 instances (16 per cent) 1 of these being incomplete Of these 3 instances were associated with previous cardiac operations although 1 was in the patient with constrictive pericarditis

At operation, 31 (46 per cent) of the 67 patients showed unequivocal and 6 showed possible increased myocardial irritability Twenty five patients, or 37 per cent of all the deaths showed ventricular fibrillation or cardiac arrest during surgery Of these, 7 were resuscitated but died in the immediate post operative period

Among the 25 operating room cardiac arrests or instances of ventricular fibrillation, 10 were associated with unequivocal evidence of sudden or severe blood loss The median blood replacement in these 10 cases was 2,500 c c , with a range of 1,000 plus to 5,000 c c Despite the fact that considerable care was taken to replace blood loss, these patients tolerated even small deficits very poorly A definite diminution in blood pressure (either abrupt or gradual) occurred in 19 (76 per cent) from 4 to 30 minutes preceding cardiac asystole The blood pressure fall started with inception of anesthesia in 1, with placement in the lateral position in 1, on opening the pericardium in 5, with cardiac instrumentation or manipulation in 8, and with sudden blood loss in 2 There was no hypotension in 6 and, in 2 in which the aorta was cross clamped, there was hypertension Cardiac asystole occurred in the intrathoracic part of the operation in 15 instances, and after completion of that portion of the operation in 10 Eleven had evidence suggestive of digitalis toxicity and all 25 showed myocardial irritability Intravenous procaine or procaine amide was used as an emergency measure in 14 instances. In 12 of the 25 patients, measurement of left ventricular end diastolic pressure was performed and showed a median of 20 mm. Hg and a range of 12 to 44 mm. Hg.

It is interesting that of 22 patients who died in the first 48 hours after surgery, 20 (91 per cent) showed shock as part of the death picture, and 6 (27 per cent) showed frank congestive heart failure. (The shock and congestive heart failure were primary entities following surgery and not merely terminal events.)

It is also interesting that all 4 immediate postoperative deaths following mitral commissurotomy were associated with cerebral emboli.

Of 27 patients who died later than 48 hours after operation, 15 showed shock in the immediate postoperative period and 24 (89 per cent) showed frank congestive failure.

CONCLUSIONS

The data suggest that cardiac asystole, the cause of the operating room deaths, is associated with sudden or severe blood loss, definite periods of prearrest hypotension, increased myocardial irritability, and increased left ventricular end-diastolic pressure. The immediate postoperative deaths seem predominately related to post-surgical shock and to a lesser extent, frank congestive cardiac failure. The delayed postoperative deaths are almost invariably related to the presence of frank congestive failure. In most cases the shock and the congestive failure (not merely terminal events) were related to one or a combination of the following: (a) failure of the myocardium, despite good mechanical correction of the lesion, (b) aggravation of a pre-existing lesion, (c) production of a new lesion, and (d) failure to correct the mechanical lesion.

The exact place, in the above scheme, of other factors, such as digitalis toxicity, rheumatic activity, pericarditis, and myocardial dilatation or hypertrophy is limited by our lack of knowledge pertinent to these phenomena. Far-advanced tissue damage and anatomic derangements of the valves themselves, of the myocardium and of the pulmonary vasculature, are, at present, major insurmountable obstacles in the practice of cardiac surgery.

SUMMARY

A review of 67 consecutive closed cardiac surgical deaths, occurring over a 5-year period, is presented.

Major groups consisting of patients with acquired valvular heart disease are compared.

Some general correlations relating the types of cases, types of operation, the time intervals between significant events in the clinical course, various factors appearing to have a role in the death of the patient, considerations of a technical nature, and all available objective data of a physiologic or of a pathologic character have been attempted.

Some general conclusions are suggested.

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DISCUSSION

DR. GABRIEL P. SELEY (New York, N. Y.).—I would like to mention a complication that we have experienced in cardiac surgery, that is, gastrointestinal bleeding, especially in children. This work is from the service of Dr. Baronofsky, Mount Sinai Hospital, and was reported in the March-April issue of the *Mount Sinai Journal* by Drs. Kreel and Zaroff.

The first case was that of a 13-year-old boy who had a huge patent ductus successfully divided and sutured. On the fifth postoperative day he developed massive hematemesis and melena. He required 2,500 c.c. of blood. Nine hours later he bled again, required another 2,000 c.c. of blood, and about half an hour later developed evidence of massive perforation into the abdominal cavity and died.

Postmortem showed an acute perforated gastrointestinal ulceration with bleeding and perforation as the cause of death. The patent ductus was successfully closed.

In addition to this, there was a 14-year-old boy who had an interatrial septal defect closed with cardiopulmonary bypass. On the twenty-first day postoperatively he developed gastrointestinal bleeding and required 2,500 c.c. of blood over a period of 7 days, and finally recovered. X-rays showed a healed duodenal ulcer.

The next case was that of an 11-year-old boy with congenital aortic stenosis successfully repaired with cardiopulmonary bypass, who, on the second postoperative day, had massive tarry stools, required 1,000 c.c. of blood, and recovered.

The fourth case was that of a 17-year-old girl who had an interatrial septol defect successfully closed, who, on the fourth postoperative day, developed gastrointestinal bleeding not requiring transfusion.

The fifth case was that of a 37-year-old man who had a right atrial tumor removed successfully with the use of a pump. On the seventh postoperative day, he had 2,000 c.c. of gastrointestinal bleeding and he finally recovered.

We mention these cases because one should be careful to observe the patients carefully postoperatively, transfuse them if necessary and, if absolutely indicated, operate to stop the hemorrhage.

DR. JULIO C. DAVILA (Philadelphia, Pa.)—It is our feeling, likewise, that there is very little to discuss in this sort of presentation.

In undertaking this review, it was hoped that some overlooked factors, something perhaps that we have been missing in our day-to-day experience, might have turned up. As it is, our findings are in very general agreement with our day-to-day experience, and I am sure with that of most of us. They confirm that the lessons that we learn on each case are generally valid observations.

Dr. Seley's remarks about gastrointestinal bleeding are of interest. We have not seen a significant incidence of this complication. I recall at the moment only 2 cases in our entire experience, 1 operated at a hospital other than that from which these cases are derived. This patient had a resection of a left ventricular aneurysm performed by Dr. R. P. Glover and died on the tenth postoperative day of peptic bleeding.

The other one, a little girl who was at Presbyterian Hospital after having surgery for mitral insufficiency and after having a hemorrhagic gastrointestinal problem postoperatively, recovered without further complications.

The word this year is, "It's the pathology that counts." This is the lesson that we have all learned in the past 10 years of cardiac surgery. We must continue our efforts to identify and realistically appraise this pathology and so operate on those for whom we can accomplish something, and save some patients, for whom we can obviously do very little, from the trials and tribulations of surgery.

THE USE OF STEROIDS FOR THE CONTROL AND PREVENTION OF SERIOUS RESPIRATORY EMBARRASSMENT DURING AND AFTER INTRATHORACIC OPERATIONS

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AN INCREASING number of patients with greatly diminished lung function are seeking surgical treatment for a variety of intrathoracic lesions The respiratory impairment may be apparent before surgery, it is frequently due to bronchial asthma, emphysema or a combination of both In other patients demonstrating good pulmonary function before surgery, accidents sometimes happen, such as aspiration pneumonitis and atelectasis that may seriously embarrass respiration In still others an unusual form of respiratory distress may occur that is characterized by intractable bronchospasm, usually precipitated by periods of hypoxia and hypercapnia This report is concerned with our experience with the use of various steroid compounds to control and prevent respiratory embarrassment in 26 such patients subjected to a variety of intrathoracic operations

MATERIALS

The patients were divided into four categories In the first category (Table 1) were patients with asthma that was nearly always associated with moderately severe to severe emphysema These patients were prepared for surgery with the steroids given in amounts ample to relieve all asthmatic wheezes if these were present, even though large doses had to be given over several days' time In the postoperative period the steroids were continued for 2 to 7 weeks One patient in this group had had bleeding from reflux esophagitis associated with hiatus hernia as well as a history of a duodenal ulcer No complications occurred in this individual Five patients were submitted to surgery because of large space consuming emphysematous cysts There were no persistent air leaks or difficulties with wound healing Two of the patients had maximum breathing capacities below 30 per cent of normal A tracheotomy was done in all 5 of the patients with emphysematous cysts The following case history is cited as an example of the patients placed in this category

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TABLE I. GROUP I: CONTROL OF ASTHMATIC ATTACKS WITH STEROIDS IN PATIENTS SUBMITTED TO A THORACOTOMY

NO.	SEX	AGE	DIAGNOSIS	OPERATION	COMMENT
1	M	41	Hiatus hernia; repeated hematemesis	Repair	Asthma controlled
2	F	60	Granuloma of lung	Excision of subsegment of lung	Asthma controlled
3	M	50	Middle lobe bronchiectasis	Middle lobectomy	Asthma controlled
4	F	10	Middle lobe bronchiectasis	Middle lobectomy	Asthma controlled
5	M	50	Severe emphysema; lung cyst	Resection of cysts	Preoperative MBC = 28% of normal; no complications
6	M	78	Carcinoma of lung	Anterior segmental resection of upper lobe	Asthma controlled
7	M	67	Severe emphysema; lung cyst	Resection of cyst	Asthma marked; controlled, MBC = 64.7% of normal
8	M	58	Recurrent pneumothoraces	Excision of apical cyst	Asthma controlled; MBC = 27.6% of normal
9	M	54	Lung cyst; emphysema	Resection of cyst	Asthma controlled; preop. MBC = 56% of normal
10	M	64	Mediastinal lymphosarcoma	Anterior thoracotomy and biopsy	Asthma controlled

CASE I.—The patient, a 67-year-old man, had suffered from bronchial asthma for 10 years. In the last year the attacks of asthma were associated with alarming episodes of cyanosis and respiratory distress requiring many hospitalizations for the administration of oxygen. X-ray studies revealed a large emphysematous cyst in the right upper lung field which compressed more than 50 per cent of the right lung. There was also a smaller cyst on the left. On admission, the patient's maximum breathing capacity was 64 per cent of normal. The residual capacity to the total capacity ratio was 46.3. Helium clearance was 6 minutes. This patient was prepared for excision of the cyst in the right lung with 40 mg. of prednisone daily. During the operation and for the first 3 postoperative days, he was given 200 mg. of cortisone acetate intramuscularly, and then shifted to prednisone 40 mg. daily. At operation, a large emphysematous cyst was removed. A tracheotomy was performed in the operating room as a further safety measure and allowed to remain in place until the sixth postoperative day. Since this patient was a severe asthmatic, he was discharged with instructions to take 20 mg. of prednisone, 2 per day for 4 weeks. He was then to gradually taper off the drug dosage for a period of 2 weeks. The patient's postoperative course was entirely uneventful.

In the second category (Table II), the patients had marked emphysema, but they did not give a history of asthma or other evidence of allergy. One patient with a hiatus hernia was 85 years of age, while 2 others were over 75 years of age. Steroids were begun 24 hours before surgery and discontinued after 5 to 21 days. In none of the group were there any cardiovascular, pulmonary, or gastrointestinal complications following surgery. A patient's history is outlined below to illustrate the method of handling this group of patients.

TABLE II GROUP II PATIENTS TREATED WITH STEROIDS BEFORE AND AFTER SURGERY BECAUSE OF EMPHYSEMA AND ADVANCED AGE

NO	SEX	AGE	DIAGNOSIS	OPERATION	COMMENT
1	M	80	Carcinoma of esophagus	Exploration of mediastinum	No postop complications
2	M	75	Carcinoma of lung	Superior segmental resection	No postop complications
3	F	85	Hiatus hernia, hematemesis	Repair of hernia	No postop complications
4	M	51	Emphysema carcinoma of lung	Biopsy of carcinoma of lung	No postop complications
5	M	46	Moderate emphysema, carcinoma of lung	Left pneumonectomy	No postop complications [illegible]
6	M	64	Emphysema, carcinoma of lung	Biopsy of carcinoma of lung	No postop complications

CASE 2—The patient, a woman, was 85 years of age and had had symptoms of indigestion, regurgitation of stomach content, and heartburn for 10 years Two years before admission she fractured her hip and had been bedridden since that time Because this condition required almost constant bed rest, her symptoms were greatly aggravated In addition to heartburn, she had acute episodes that were characterized by severe epigastric pain, nausea, and vomiting of coffee ground material Morphine and constant aspiration of the stomach with an indwelling nasogastric tube were necessary for relief In spite of the patient's age, it became necessary to repair the large hiatus hernia The patient was then given cortisone acetate, 100 mg intramuscularly twice daily, for 3 days before surgery Using general anesthesia, the hiatus hernia was repaired through a left thoracotomy incision Following operation, the patient was continued on 200 mg of cortisone acetate daily for 3 days She was then given prednisone, 10 mg 4 times a day for 5 days After this, the steroid was gradually reduced until finally, after 10 days, it was discontinued altogether This patient's postoperative course was not complicated by either respiratory, cardiovascular, or gastrointestinal symptoms

In the third group of 6 patients (Table III), the indication for the steroids was to control the infection that followed the spread of secretions into the nonoperated lung that occurred during anesthesia In 3, this was due to partial collapse of the operated lung and the squeezing out of secretions into the tracheobronchial tree with inadequate suction during the course of the operation In 3, the spread was due to tuberculosis, while in 1 it was from coccidioidomycosis The most striking physical sign was profound respiratory embarrassment accompanied by many expiratory wheezes With the intravenous administration of 100 to 400 mg of hydrocortisone, the relief was dramatic in all instances The patient with coccidioidomycosis eventually died of disseminated disease There was 1 patient of the 3 with tuberculosis who died but this was not due to a dissemination of the disease but to coronary thrombosis The following case history is an example of the patients in this category

CASE 3—The patient a man, was 63 years of age and had a suppurative lung lesion of 3 months' duration due to an unknown pyogenic organism This had been treated vigorously all this time with antibiotics, but there still remained a large thick walled cavity

TABLE III. GROUP III: PATIENTS WHO RECEIVED STEROIDS IN POSTOPERATIVE PERIOD FOR ACUTE DISSEMINATED BRONCHOPNEUMONIA

NO.	SEX	AGE	DIAGNOSIS	OPERATION	COMMENT
1	M	71	Coccidioidomycosis	Exploration for carcinoma of lung	Died 3 weeks postop. of disseminated infection
2	M	56	Pulmonary tuberculosis	Excision of superior segment	Died 10 days postop. from coronary occlusion
3	M	46	Pulmonary tuberculosis	Segmental resection	Recovery
4	F	60	Pulmonary tuberculosis	Segmental resection	Recovery
5	M	63	Pyogenic abscess	Right middle and upper lobectomy	Recovery
6	M	50	Pulmonary tuberculosis	Upper lobectomy	Recovery

The question of carcinoma was not completely resolved, so excision was undertaken. At operation, a large abscess involving the right upper and middle lobe was removed. It was noted immediately after operation that the patient was in marked respiratory distress and that he did not improve in spite of frequent aspirations and positive pressure oxygen. He was noted to show extreme expiratory effort and loud expiratory wheezes were audible. A tracheotomy was then performed, but this resulted in only slight improvement. Because of continued respiratory distress and cyanosis, he was given an injection of 200 mg. of hydrocortisone intravenously and then given 200 mg. more in an intravenous drip over the next 12 hours. This resulted in immediate and dramatic improvement in the patient's respiratory symptoms. All of the expiratory wheezes disappeared, and the cyanosis showed gradual improvement over the next 2 hours. After the first 12 hours, the patient was carried on intramuscular cortisone acetate, 100 mg. twice daily, and, after the seventh day, this was gradually withdrawn until he was off steroids entirely at the end of 2 weeks. Erythromycin, 1 Gm., and 1,600,000 units of penicillin were given each day. The patient made an uneventful recovery in spite of the fact that x-ray studies showed diffuse bronchopneumonia throughout the unoperated side. This condition eventually cleared completely, and there was no residual infection or disease in either the operated or unoperated lung.

In the fourth group (Table IV) were patients who developed severe bronchospasm either during surgery or in the early postoperative period. These patients denied ever having had asthma. In 2 instances, the onset of the expiratory obstruction occurred more than 48 hours after surgery and was associated with proved respiratory acidosis. In both instances the bronchospasm could not be corrected with aminophyllin and epinephrine, but it did respond to large doses of intravenous steroids. As soon as the bronchospasm was corrected, the blood gas and pH studies returned to more normal levels, and the other signs of respiratory acidosis, such as clouded sensorium, unconsciousness, and arterial hypotension, disappeared. In one instance, the initiating factor was inadequate ventilation which prevented the unoperated lung from being adequately aerated. The bronchospasm developed during the time of surgery. In spite of the fact that the position of the endotracheal tube was corrected and the chest was closed, the persistent bronchospasm was not relieved until 400 mg. of hydrocortisone was administered intravenously. In another instance the patient had a large intrathoracic tumor that interfered with ventilation. This was followed by bronchospasm that was corrected by the intravenous administration of 200 mg. of hydrocortisone. The patient, who had cirrhosis of the liver, eventually succumbed [illegible] liver failure. The following summary is an example of the employment of cortisone in this group of patients.

TABLE IV. GROUP IV. PATIENTS TREATED WITH STEROIDS IN POST[illegible] DURING OPERATION BECAUSE OF ACUTE RESPIRATORY EMBARRASSMENT ASSOCIATED WITH INTRACTABLE BRONCHOSPASM

NO.	SEX	AGE	DIAGNOSIS	OPERATION	
1	M	42	Esophageal varices, cirrhosis of liver	Ligation of esophageal varices	Respir[illegible] days [illegible] died 28 [illegible] liver failure
2	M	49	Hiatus hernia, recurrent	Attempted repair, malplaced endotracheal tube	Intense bronchospasm only relieved by 400 mg. of I.V. cortisone, recovery
3	M	58	Carcinoma of lung	Pneumonectomy	Respiratory acidosis, recovery
4	M	62	Carcinoma of lung	Biopsy of carcinoma of lung	Bronchospasm, relieved in O.R. by 200 mg. I.V. cortisone

CASE 1.—The patient was a 43-year-old white man admitted to the hospital with a history of repeated gastrointestinal hemorrhages that had begun suddenly 3 weeks before. Finally, after 1 week of observation in his local hospital, the abdomen was explored for a possible bleeding peptic ulcer. At this time the stomach and duodenum were normal, but the patient was found to have marked cirrhosis of the liver. A balloon tampon was passed into the esophagus and stomach, and the hemorrhage was then well controlled. After 2 days, it was removed, but the hemorrhage recurred, and for this reason the patient was transferred to Duke Hospital with the tampon still in place. After the abdominal operation, a tracheotomy had been done. Twelve hours after admission to Duke Hospital, a left thoracotomy was carried out with exploration of the esophagus and intraesophageal ligation of esophageal varices. The response to surgery was satisfactory in spite of the fact that he had had a previous abdominal operation, was markedly overweight, and was intensely jaundiced. On the seventh day after operation, he was noted to be [illegible] comatose but without evidence of recurrent bleeding and with no obvious deterioration in liver function. On examination of the chest, breath sounds were quite distant except for very faint expiratory wheezes. It was suspected that he had respiratory acidosis. Arterial carbon dioxide tension was found to be 101 mm. of mercury. The pH was 7.32 and oxygen saturation was 82 per cent. Artificial ventilation with a mechanical ventilator through a cuffed endotracheal tube was started and 200 mg. of hydrocortisone given in 1 dose intravenously with another 200 mg. allowed to drip in slowly. In the next 24 hours the patient's sensorium cleared markedly and breath sounds became more normal, although it was of interest that, as the ventilation became more effective, more expiratory wheezes could be heard. After 24 hours, ventilation was excellent and the respiratory wheezes had disappeared. The arterial pCO_2 had diminished to 77.[illegible] mm. of mercury with a pH of 7.35 and an oxygen saturation of 100 per cent. Six days later the findings were further improved, the pCO_2 being 70 and the pH 7.39. Cortisone was continued for 10 more days, being tapered off in the latter part of this period until at the end of this time no more steroids were administered. The patient, however, succumbed [illegible] weeks later from progressive liver insufficiency.

TABLE III. GROUP I
F

NO.	SEX	AGE	
1	M	71	Coccidi
2	M	56	Pulmona
3	M	46	Pulmona
4	F	60	Pulmonary
5	M	63	Pyogenic a
6	M	50	Pulmonary t

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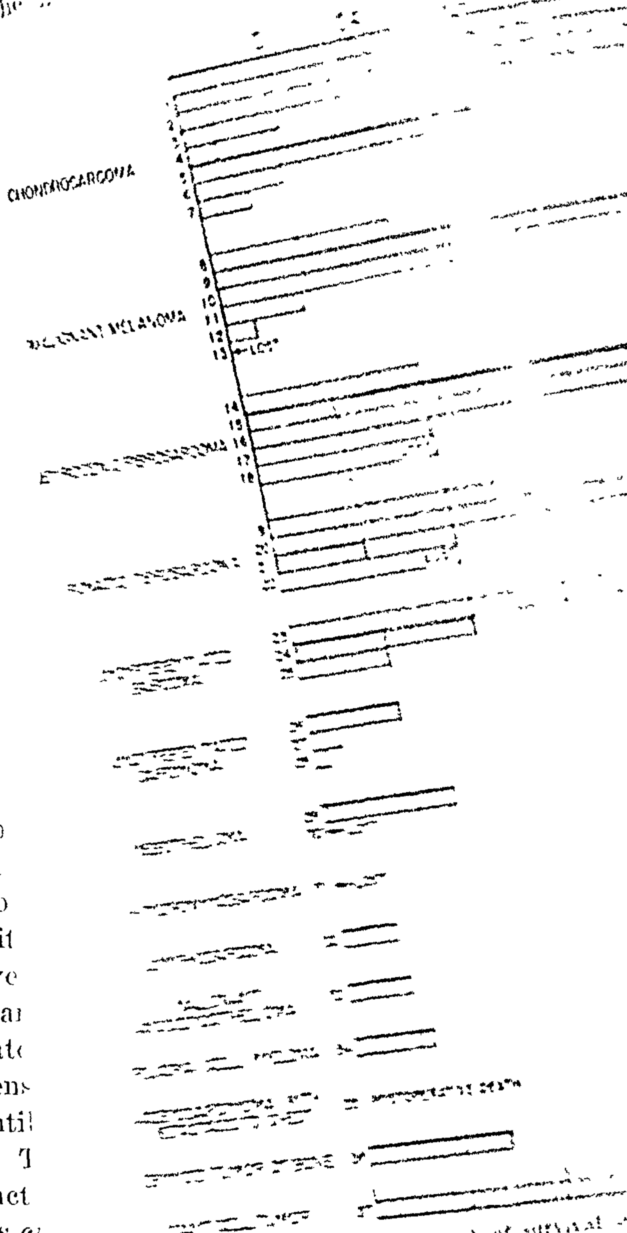

may result in bronchospasm, and our experience indicates that respiratory acidosis cannot be relieved until the bronchospasm is controlled.

The steroids also have a beneficial nonspecific effect that is difficult to pinpoint but does allow support to the debilitated patient As a result of our favorable experience with the patients in this study who were debilitated, we have extended the use of steroids to more and more poor-risk patients The sense of well being, the lack of respiratory complications, and the control of fever have made this drug a most valuable adjunct to surgery of the chest in the aged and debilitated

There are certain toxic effects of steroids that have to be considered, and it has been this fear perhaps, that has prevented the more widespread use of these drugs in surgery The principal complications come from prolonged usage Administered over a few days' time, as in the nonasthmatics of our group, there is very little chance that there will be a significant reduction in the resistance to infection or a significant effect on wound healing[6] It is also of great interest that where there has been acute tuberculous pneumonia, the steroids have served to tide the patient over for a few days and they have not, in our opinion interfered with the control of the infection with appropriate antibiotics

No gastrointestinal bleeding has occurred in any of the patients, in spite of the fact that many patients were emphysematous and some had a previous history of gastrointestinal bleeding To reduce the possibility of peptic ulceration, the stomach was aspirated after operation, and this was continued until good gastrointestinal function returned

There have been no significant electrolyte disturbances except in those patients who already had respiratory acidosis, and this has tended to be corrected as the respiratory acidosis has been relieved Daily electrolyte studies have been done on most of these patients in the postoperative period

Based on our experience *we now use steroids in the preoperative, operative,* and postoperative periods in known asthmatics In patients who have poor pulmonary reserve the steroids are always used as a preventative In elderly patients who, in addition to moderate emphysema, frequently have a moderate amount of debility, the help of steroids is used to carry them through operation

Where marked bronchospasm develops during the course of the operation, such as we have noted in respiratory acidosis, intravenous steroids are given until the bronchospasm is corrected and good ventilation is obtained In acute respiratory emergencies, where there is disseminated spotty atelectasis and bronchopneumonia, large doses of steroids are given intravenously along with appropriate antibiotics

SUMMARY

The experience with 26 patients given steroids for either prevention or control of respiratory impairment after thoracotomy is reviewed In none of the patients have complications occurred from the steroid therapy. In some,

with serious respiratory embarrassment, elective operations have been made possible by the prophylactic use of steroids. In others, who developed acute diffuse bronchopneumonia after operation or who developed respiratory acidosis with bronchospasm, it is believed that the steroids have been lifesaving.

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MALIGNANT TUMORS INVOLVING THE CHEST WALL

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AS THE GENERAL public has become increasingly aware of the importance of early diagnosis of cancer, an increasing number of patients with chest wall tumors have come to this clinic for treatment During the period 1938 to 1958, a total of 339 patients were seen In 302 of these cases, the masses represented benign growths, including nevi, lipomas, exostoses, and so forth, but in 36 instances the tumor was malignant In one other case the initial histologic diagnosis was osteogenic sarcoma of rib, but after further biopsy study, the diagnosis of benign giant cell tumor of the bone was made This case is included to indicate the problems inherent in the diagnosis of these tumors

In addition to the usual growths of mesenchymal origin involving the somatic soft tissues of the thoracic wall, we have included melanomas and mesotheliomas which invaded soft tissue and a variety of bone tumors which, of necessity, had to be differentiated from soft tissue lesions by careful roentgen and biopsy study Although the characteristics of such a conglomerate group of tumors vary considerably certain clinical features are common to all, and this renders precise diagnosis impossible without careful roentgenologic and histologic study Despite the varying cellular origins of these masses, treatment does not vary greatly, wide excision and selected radiation therapy are utilized in most cases

As is common in surveys of this type,[1-4] the cell types varied so widely that the number of patients in the series with a tumor of one type was small, and over all survival figures are thus meaningless The various cell types encountered, together with follow up results in each case, are presented in Fig 1

AGE AND SEX DISTRIBUTION

The median age of a patient at the time of initial diagnosis ranged from 40 to 49 years with extremes of age from 14 to 69 years (Fig 2) Only 2 patients were under the age of 20 The series included 25 men and 12 women No connection between the development of thoracic tumors, and occupation or co existing disease was apparent

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SYMPTOMS

The appearance of a painless mass on the thoracic wall was the most common reason for a patient to seek medical attention, being the cause of initial complaint in 20 of the 37 patients. Pain was apparently a later symptom, but was the initial complaint in 13 patients. Miscellaneous causes for seeking medical attention included shortness of breath in 2 patients with pleura encroachment, cough in 1 patient, and change of growth characteristics in a mole indicating the development of malignant melanoma in another instance. It would appear that, in general, the longer a symptom was present before operation, the longer that patient survived after treatment—suggesting that such

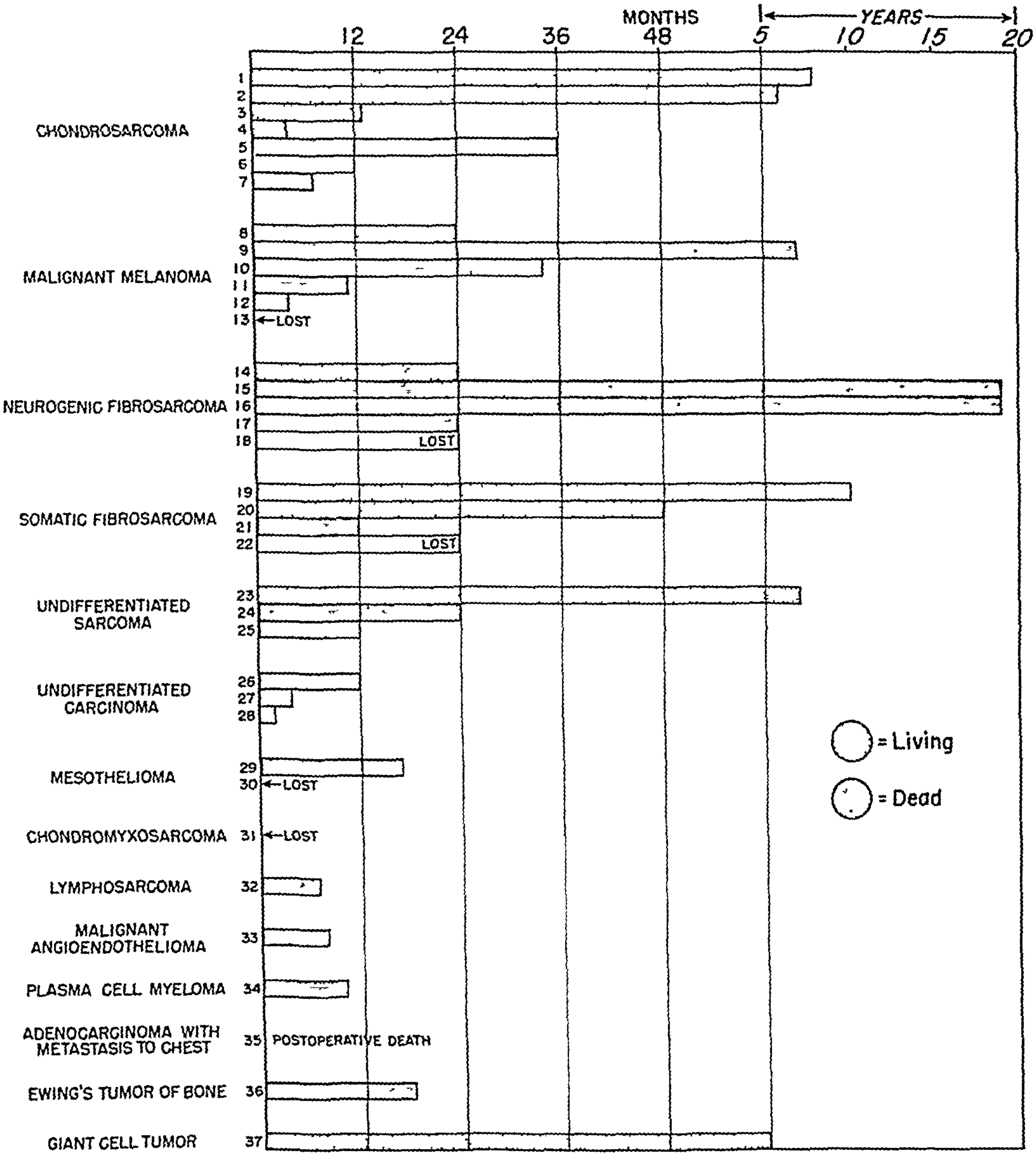


Fig 1.—Length of survival according to cell type of tumor.

tumors grew slowly and were less likely to extend early beyond the confines suitable for adequate surgical or radiation therapy In 3 cases, the development of a chest wall tumor was preceded by the development of an unrelated malignant lesion appearing years before the onset of the disease in the thoracic wall A biologic tendency to the development of malignant disease may have been present in these cases

DEFINITIVE DIAGNOSIS OF THE MASS

Since a painless lump was the most common presenting complaint, physical examination usually sufficed to establish the fact that a tumor was present but histologic examination was essential before an effective therapeutic plan could be formulated Whether histologic diagnosis was established by study of an incisional biopsy specimen or by block excision was governed by the size of the lesion, the clinical features indicative of the possible cell type, and the general physical condition of the patient Since radical surgical excision is the most satisfactory therapeutic method in the majority of these cases, our efforts have been directed chiefly toward preparation of patients for initial radical excision, biopsy study has been reserved for the few questionable lesions of large size in refractorily debilitated patients with metastases or for those patients who might be expected to derive maximum benefit from an initial course of two million volt radiation therapy

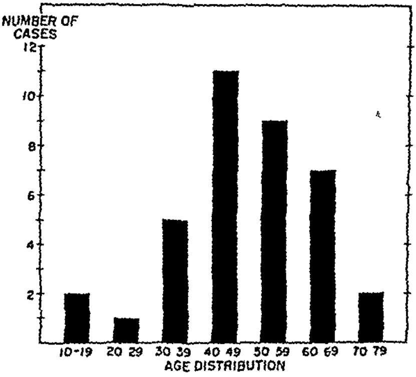


Fig 2 —Age distribution

Before any surgical procedure is undertaken, be it biopsy or excision, a roentgenogram of the chest should be made Further radiographic studies may be required to rule out the presence of a metastatic process

Rapid frozen microsection is of limited value in these cases because of the subtleties of histologic diagnosis, and because bone and cartilage elements so frequently preclude this method of tissue sectioning All biopsy incisions are closed meticulously It is doubtful that a delay for paraffin microsection intro duces an appreciable hazard of metastasis, since any subsequent excision of a radical nature would encompass the entire area of biopsy. We have not used needle aspiration biopsy, preferring to have the greater bulk of tissue obtained by incisional biopsies available for study.

MICROSCOPIC CLASSIFICATION

In most of the groups, the definition of cell type follows a conventional type of classification. However, the fibrosarcomas have been divided into a somatic group, representing those tumors obviously arising from the fibrous components of muscle and connective tissue, and a neurogenic fibrosarcoma group, representing tumors arising from the stromal elements of nerves. The latter group has been classified by other pathologists as representing sarcomatous change within the neurilemmal sheath, and hence the term "neurilemmoma" has been applied to such lesions.

The undifferentiated sarcoma group either presented such an anaplastic picture that the origin of the characteristic cell type could not be determined, or represented highly malignant growths in which areas of different types of sarcomatous degeneration could be found (for example, anaplastic tumors containing elements of liposarcoma and fibrosarcoma). We believe that such undifferentiated sarcomas represent anaplastic lesions with multipotential growth characteristics.

MANAGEMENT

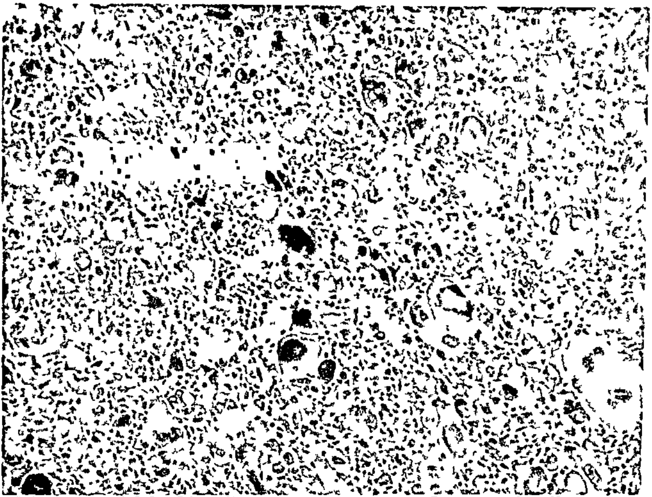
Every attempt has been made to obtain a wide block excision of the primary growth at the time of operation. Such excisions frequently required the removal of segments of ribs, costal cartilages, or sternum, either because of deep invasion of the more superficial tumors or because the tumor arose directly from these structures. In no instance was amputation of the shoulder girdle required.

Local recurrence was frequent in the various groups, particularly when the initial excision elsewhere had been patently inadequate. In a number of such cases, re-excision was possible and added appreciably to the survival time. Two patients in the fibrosarcoma group were submitted to re-excisions over a period of 2 to 4 years, and 1 of these is still living 2 years following a second excision for recurrence. A number of the block excisions involved the excision of multiple ribs and intercostal bundles. Prior to 1950, no attempt was made to apply struts or supports into the resulting extensive defect in these cases. Oddly enough, lung herniation did not appear to be a problem.

A small lump in a healthy, young patient would be considered favorable for complete eradication by excision biopsy with a generous margin of normal tissue, whereas large masses encroaching on thoracic viscera in a patient in poor physical condition would be sectioned for biopsy study during preparation of the patient for definitive excision, radiation therapy, or both.

The major error that arises in the management of these tumors, as in most mesenchymal tumors of the somatic soft parts, results from failure to make a

Fig 3



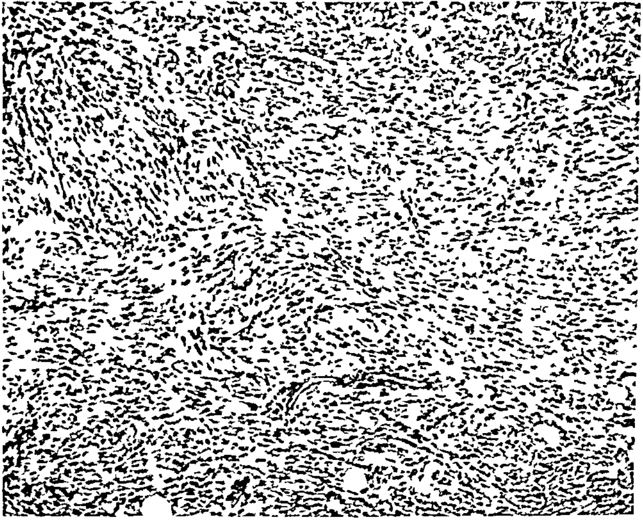


Fig 4

Fig 3.—Undifferentiated sarcoma Pleomorphism of cell elements and lack of characteristic architecture indicate the difficulty encountered in attempting to classify this type of tumor (Hematoxylin and eosin, ×125, reduced ⅕)

Fig 4.—Fibrosarcoma, somatic type Proliferating fibroblasts show irregular whorls without the palisade alignment characteristic of the neurogenic type (Hematoxylin and eosin; ×125, reduced ⅕)

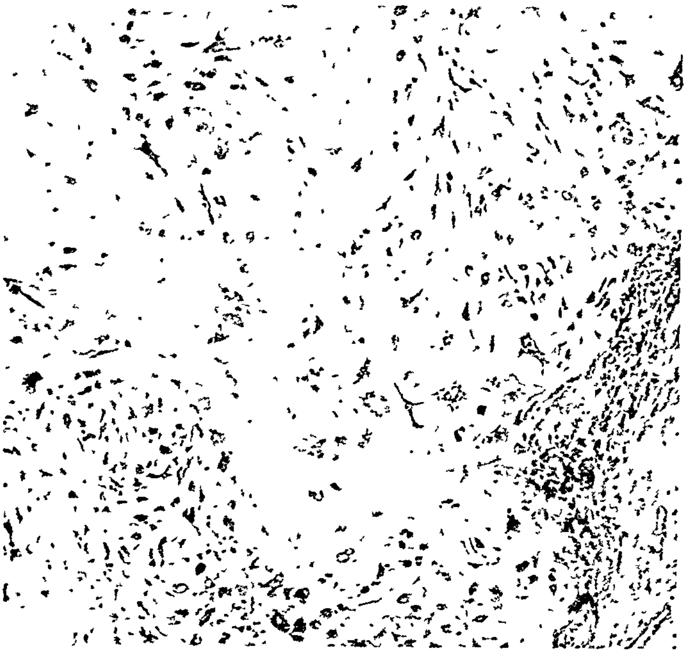


Fig. 5.—Chondrosarcoma. Characteristic distortion of cellular elements. (Hematoxylin and eosin; ×100; reduced ⅕.)

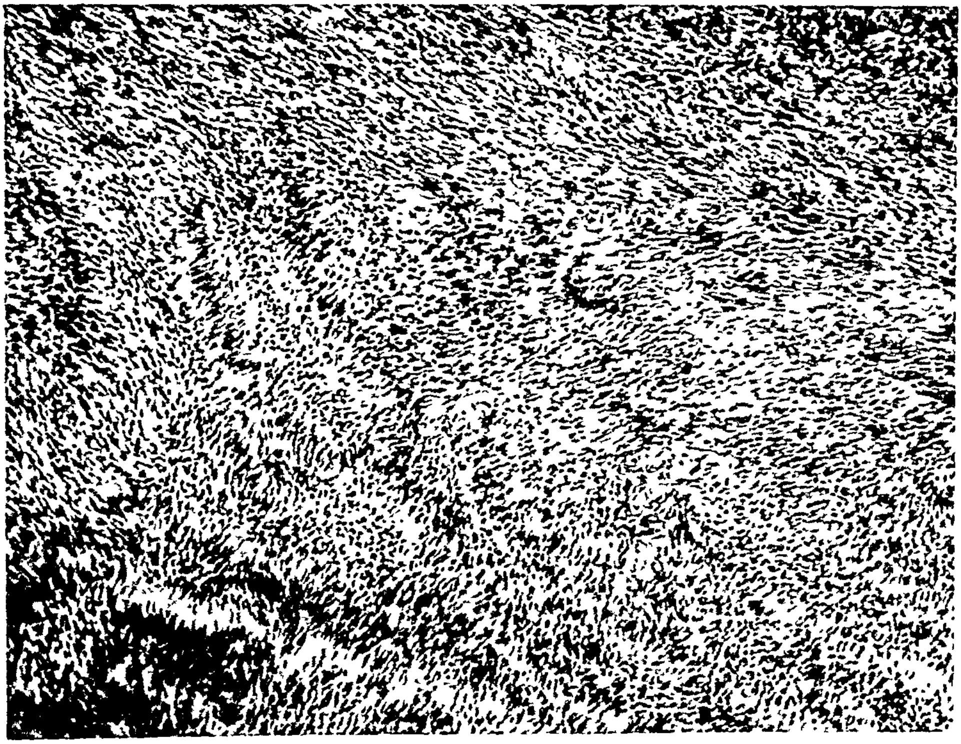


Fig. 6.—Neurogenic fibrosarcoma. This tumor is typified by the palisading arrangement of the fibroblasts which are thought to arise from the fibrous elements of nerve sheaths. (Hematoxylin and eosin; ×125; reduced ⅕.)

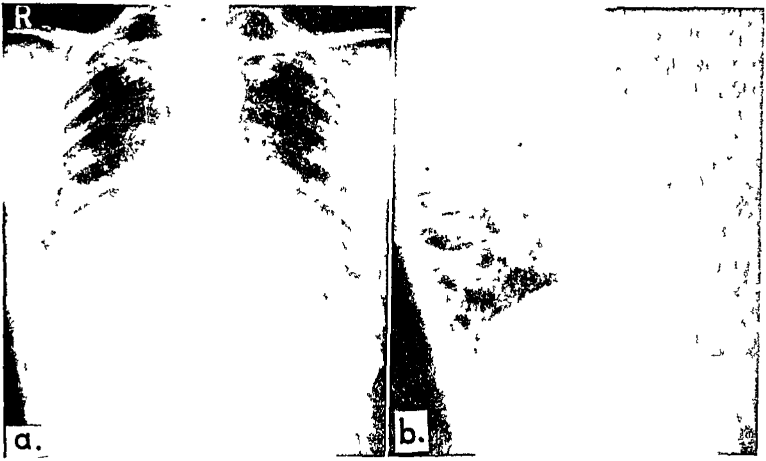


Fig. 7.—Posteroanterior (*a*) and right lateral (*b*) views in 62-year-old man showing chondrosarcoma of costal cartilage. Mass was excised by block excision of ribs 6, 7, 8 and 9, lower sternum and segment of diaphragm.

Fig. 8.—Lateral view showing chondrosarcoma of sternum. Manubrium, upper two thirds of body of sternum, medial half of each clavicle and anterior segments of ribs 1, 2 and 3 were later excised en bloc to remove mass.

sufficiently wide excision at the initial operation. The thoracic wall presents certain problems in the excision of complete muscle bundles, in view of the broad origin of the pectoralis major muscle anteriorly and resultant hesitation concerning excision of the entire muscle when this is involved by tumor. Moreover, the surgeon is reluctant to create large thoracic defects for fear of jeopardizing the patient's welfare in the immediate postoperative period by the creation of ventilatory insufficiency. This conservatism may result in unnecessary recurrence of tumor masses, and re-excisions in such areas are extremely difficult. It should be emphasized that wide primary excision is feasible and safe when applied to the thoracic wall. It should be possible to restore the integrity of the chest wall with suitable periosteal strips, autogenous bone grafts or temporary external supports but, even if this is not feasible, the body has a remarkable ability to adapt to extensive bony defects of the thoracic cage. This is strikingly illustrated in the following case report.

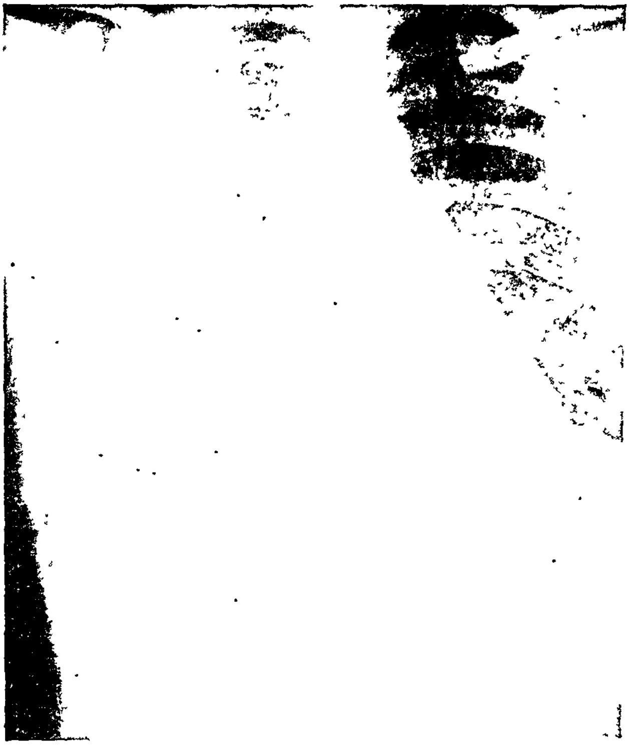


Fig. 9.—Posteroanterior roentgenogram made on sixth postoperative day, following excision of sternum, clavicle, and ribs as described in Fig. 8.

REPORT OF CASE

A 34-year-old mechanic first came to the clinic in 1951. He complained of a mass below the clavicle, which had been increasing in size for a period of 3 months before admission. Radical excision of this mass—a chondrosarcoma of the second costal cartilage—was carried out the same year. The manubrium of the sternum was removed in continuity with the upper two thirds of the body of the sternum, the medial half of each clavicle, and anterior segments of the first, second, and third ribs on each side. Severe respiratory difficulty followed this operation as a result of paradoxical motion of the flail chest wall This was treated only by a tight dressing and tracheobronchial catheter aspiration, although at the present time we would favor more vigorous therapy such a external fixation and early tracheostomy Approximately 500 c c of serous material was removed from the wound but the patient was well on the road to recovery by the twenty second postoperative day By the sixth week after operation the flail area of the thorax wall was apparently stable Sixteen months after operation, the patient was lost to follow up During the follow up period, he showed no evidence of tumor recurrence however

The first information we had concerning the patient's ability to perform work following this extensive resection was obtained in a letter received 5 years after operation, in the course of preparation of this manuscript Since it indicates better than any technical description the end result obtained without the use of struts, we have published the letter here in its entirety

> Dear Doctor
>
> In regard to your letter concerning my operation about six years ago, I had to be very careful about straining my chest Standing up right I could do a normal day's work, but if I had to be under a truck and lift anything while on my back I would be useless Standing to put my hands behind my head was uncomfortable and at times painful
>
> About a year or so ago, I was under a truck, it slipped off the jack and pinned me on the upper part of my chest within 6 inches of the floor I lost about two weeks' work and then discovered as I regained my strength that I could put my hands behind my head, or lie on the floor and lift heavy objects without discomfort
>
> The last year I have been driving a motorcycle, it does not affect me in any way My occupation is a truck mechanic—heavy equipment, and I now weigh about 180 pounds The remaining effect from the operation, I believe, is poor circulation in the arms when I go to bed at night only, I toss and turn a lot during the night

Although this type of physiotherapy (compression of the chest wall by a truck) is not recommended, it serves to indicate the ability of this patient to engage in active labor without discomfort or incapacity following radical excision of a malignant tumor in the thoracic wall

RADIATION THERAPY

Since 1951, we have utilized two million volt x ray therapy as an ancillary measure to wide block excision The usual tissue dose is 7,500 r In the absence of distant metastases, surgical excision was the primary form of treatment Postoperative radiation therapy is reserved for those cases in which excision is incomplete because of extension into the vertebral bodies, spinal canal, heart, and other vital areas In the presence of recurrences, a number of re excisions might be attempted before radiation is employed In the presence of distant metastases, surgical excision would be preferable to radiation therapy only if an emergency problem of ventilatory mechanics indicated that excision might possibly expedite disease control and prolong life

TABLE I. SUMMARY OF CASES

CASE	AGE AND SEX	INITIAL COMPLAINT; PERIOD TO OPERATION	TYPE OF OPERATION	POSTOPERATIVE THERAPY	FOLLOW-UP REPORT
			Chondrosarcoma		
1	34 M	Lump 4 mo.	Block excision, manubrium, body of sternum, medial clavicles, ribs 1, 2, and 3	None	Living and well 8 yr.
2	31 F	Pain 36 mo.	Excisions of ribs 4 and 5 and spinal canal extension D_{11}-L_2	7,500 r 2 mev.	Living with disease 6 yr.
3	70 M	Lump 1 mo.	Block excision, ribs 7, 8, and 9	None	Living and well 1 yr.
4	62 M	Lump 4 mo.	Block excision, ribs 6 through 9, sternum, diaphragm		Living and well 4 mo.
5	47 M	Lump 24 mo.	Block excisions, multiple, of ribs 5 and 6, and 7, 8, and 9	7,500 r 2 mev.	Died of disease 3 yr.
6	49 M	Lump 12 mo.	Block excision, rib 9	7,500 r 2 mev.	Died of disease 1 yr.
7	56 F	Lump 6 mo.	Excision, left breast, chest wall, left lung tissue	None	Died of disease 7 mo.
			Malignant Melanoma		
8	47 M	Mole	Multiple local re-excisions 2 yr., soft tissues	None	Living and well 2 yr.
9	45 M	Lump 12 mo.	Multiple block excisions 5 yr., soft tissues	None	Died of disease 7 yr.
10	40 F	Lump 5 mo.	Block excisions; supraclavicular node biopsy 2 yr.	None	Died of disease 3 yr.
11	61 F	Mole	Excision, soft tissue		Died of disease 1 yr.
12	36 M	Pain 6 mo.	Block excision ribs 2 and 3		Died of disease 4 mo.
13	67 M	Lump 1 mo.	Block excisions, soft tissues	None	Recurrence in 2 mo.; lost to follow-up
			Neurogenic Fibrosarcoma		
14	58 M	Pain 1 yr.	Excision of mass, intercostal muscle	None	Well 2 yr.
15	48 M	Lump 6 yr.	Block excision of mass and intercostal muscle	None	Died 19 yr., without recurrent disease
16	68 F	Lump ?	Block excision, rib 9	None	Died 19 yr., without recurrent disease
17	57 M	Lump 4 mo.	Multiple re-excisions, pectoralis muscle	None	Died of disease 2 yr.
18	50 M	Lump	Multiple excisions, rib 6; ribs 4 through 9; excision of recurrence	None	Lost to follow-up 2 yr.
			Somatic Fibrosarcoma		
19	44 F	Pain 18 mo.	Block excision of ribs 8 and 9		Living and well 10 yr.
20	40 M	Lump ?	Block excision; re-excision at 2 years; ribs 1 through 4	7,500 r 2 mev.	Living and well 4 yr.
21	65 M	Pain 5 mo.	Biopsy of rib 6	7,500 r 2 mev.	Died of disease 1 yr.

TABLE I—CONT'D

CASE	AGE AND SEX	INITIAL COMPLAINT, PERIOD TO OPERATION	TYPE OF OPERATION	POSTOPERATIVE THERAPY	FOLLOW-UP REPORT
22	53 F	Lump ?	Block excision, ribs 4 and 5	None	Lost to follow up 2 yr
			Undifferentiated Sarcoma		
23	59 M	Lump 36 mo	Block excision, 2 re-excisions (one year apart), soft tissues	7,500 r 2 mev	Living and well 7 yr
24	11 M	Pain 1 yr	Excision of ribs and cartilage 3	1,200 r conventional to vertebral metastases	Died of disease 2 yr
25	66 M	Lump	Excision, soft tissue	None	Died of disease 1 yr
			Undifferentiated Carcinoma		
26	42 M	Pain 4 mo	Biopsy, ribs showed undifferentiated carcinoma (from bronchus)	None	Died of disease 1 yr
27	41 F	Lump 1 mo	Block excision of sternum	None	Died of disease 4 mo
28	69 M	Pain 6 mo	Biopsy rib 11 source unknown	None	Died of disease 2 mo
			Mesothelioma		
29	46 M	Cough 1 mo	Biopsy of pleura	Radiation	Died of disease 17 mo
30	71 F	Pain 3 mo	Biopsy of pleura	Referred for radiation elsewhere	Referred, lost to follow up
			Chondromyxosarcoma		
31	30 F	Pain	Biopsy elsewhere, refused surgery	None	Lost to follow up
			Lymphosarcoma		
32	52 F	Lump 3 wk	Biopsy of rib 3	None	Died of disease 7 mo
			Malignant Angioendothelioma		
33	16 M	Shortness of breath 6 mo	Biopsy of pleura	2,400 r conventional radiation	Died of disease 8 mo, necropsy showed disease
			Plasma Cell Myeloma		
34	59 M	Pain 1 mo	Biopsy of rib 7	None	Died of generalized disease 10 mo
			Metastatic Adenocarcinoma		
35	55 M	Pain 2 yr	Block excision lung and ribs 2, 3, and 4 adenocarcinoma of lung	None	Died postoperatively
			Ewing's Tumor of Bone		
36	39 M	Cough 1 yr	Excision of ribs 8 and 9	Conventional radiation, nature unknown	Died of disease 18 mo
			Giant Cell Tumor of Bone		
37	23 F	Pain 5 mo	Biopsy of mass, excision of ribs 8 and 9 and mass, vertebral spine	1,990 r 2 mev without response, then 2nd biopsy showed giant cell tumor	Living and well 7 yr

SURVIVAL

Of the 37 patients in our series, 22 are dead, 10 are living, and 5 have been lost to follow-up (see Fig. 1). Of the 22 deaths, 20 were caused by the disease. Two patients lived 19 years after operation and died free of disease. In both of these cases, the original procedure was a block excision of a neurogenic fibrosarcoma, and further surgery was not required.

The 10 survivors are all well (the longest for 10 years) with one exception. The latter patient has metastatic disease from a chondrosarcoma and is failing. Two of the 5 patients lost to follow-up were known to be free of disease for 2 years. Although it might be reasonably safe to assume that they are still free of disease it is impossible to predict with any certainty what period of time can be considered "safe" in terms of cure; the underlying nature of the disease is the determining factor in this regard.

As we have stated previously the variety of cell types encountered and the number of cases involved in this series make analyses of survival of the over-all group relatively meaningless. Prediction of survival in any particular cell type is impossible.

SUMMARY

Between 1938 and 1958 a total of 339 patients with tumors of the thoracic wall have been seen at this clinic. In 303 of these patients the tumor was benign, but in 36 instances a malignant tumor was encountered. In addition to the sarcomas arising from the fibrous tissue or nerve elements of the thoracic wall, malignant melanomas and mesotheliomas presenting problems in management by involvement of deep structures of the thoracic wall were included, as well as a number of tumors of heterogeneous types which also presented problems in management because of their size or invasive tendencies.

Although the variety of cell types encountered in this group of 36 patients was so great as to preclude a statistically significant number of patients in any one category, it would appear that the chondrosarcomas and somatic fibrosarcomas were most amenable to treatment.

The initial presenting symptom was the appearance of a painless swelling on the thoracic wall; this was the cause for complaint in 20 of the 36 patients.

In most instances histologic diagnosis was established at the time of wide block excision of the mass. Incisional biopsy was reserved for the few questionable lesions of large size which were found in debilitated patients or patients with metastases.

At the present time, roentgen therapy, using a two million volt generator, is reserved for patients in whom distant metastasis is present, those in whom the disease was incompletely excised at the time of maximal radical surgery, extremely debilitated patients, and patients in whom a number of recurrences have been managed by re-excision.

In several instances, the local recurrence of tumors was managed by repeat excision, and these patients lived for several years following such procedures.

Patients with recurrent disease should not be abandoned but should be given every chance in view of the evidence, in a few instances here, that re excision of recurrent tumors may result in a continuation of active life over a period of years

Although the physician initially treating these lesions surgically may hesitate to excise a segment of thoracic wall wide enough to eradicate the tumor adequately, our experience indicates that conservatism in the extent of the resection is likely to lead to recurrence, and that such recurrent disease poses additional problems at the time of re excision At this time we are inclined to utilize the various techniques described for maintaining the integrity of the chest wall by the use of rib struts, periosteal strips, or external fixation A number of patients early in the series who did not have such support, however were able to acquire stability of the thoracic wall early, and went on to lead productive lives To us, the error seems greater in the lack of adequate excision than in the creation of ventilatory insufficiency following wide excisions in the thoracic wall

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SURGICAL TREATMENT OF AORTICOPULMONARY FISTULA SECONDARY TO AORTIC ARCH ANEURYSM

Report of Successful Case

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Aneurysm of the aortic arch is a serious disease which usually leads to death less than one year after the onset of symptoms.[6] In most instances the grave prognosis results from the tendency for aneurysms to encroach upon adjacent structures in the mediastinum frequently leading to rupture of the lesion with fatal hemorrhage. Perforation into the respiratory passages is apparently more frequent than rupture into vascular structures such as the vena caval system or pulmonary artery. In 1812, Wells[20] reported the first case of rupture of an arch aneurysm of syphilitic origin into the pulmonary artery producing an aorticopulmonary communication, and since that time a total of approximately 90 cases have been recorded. Thus, although the majority of syphilitic aneurysms occur in the ascending aorta where they are in intimate relationship with the pulmonary artery, it is interesting that rupture into the lesser circulation occurs in only 3 to 4 per cent of cases.[1]

Since Nicholson's[16] complete review of this subject in 1943, antemortem diagnosis of acquired aorticopulmonary fistula, secondary to aortic aneurysm, has become increasingly accurate as evidenced by the correct diagnosis in 8 of the last 10 reported cases.[2-4, 10, 12, 13, 15, 19] Onset of this complication is usually acute, with extreme dyspnea, cough, and precordial pain. Less commonly, the patient may remain relatively asymptomatic complaining only of mild dyspnea or precordial discomfort. The size of the fistula produced probably determines the severity of symptoms and clinical course. Although survival of 4 years has been reported in one case,[21] the general prognosis is poor, with survival averaging between 6 weeks and 4 months,[5] with death resulting from progressive right heart and subsequent left heart failure.[11, 17, 18]

After fistulization occurs, the anticipated signs of a shunt between the greater and lesser circulation occur. Pulse pressure widens and a water-hammer pulse becomes prominent. A thrill is often palpable over the pulmonic area of the precordium, and a continuous machinery-like murmur with systolic

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accentuation is heard in the same location Roentgenograms and fluoroscopy reveal the aneurysm with overactive pulsations in the pulmonary arteries The electrocardiogram usually reveals right axis deviation and right ventricular hypertrophy an interesting contrast to the left heart strain which occurs in the physiologically similar patent ductus arteriosus

Among the explanations for this paradoxical finding is the concept that long standing compression of the pulmonary artery, prior to rupture of the aneurysm, produces increased resistance to ventricular outflow which results in right sided hypertrophy While differential diagnoses include patent ductus arteriosus, congenital aorticopulmonary fistula, and rupture of the sinus of Valsalva, the most frequent incorrect diagnosis is thoracic aortic aneurysm with aortic insufficiency, in which the age group, etiology, physical signs, and x ray findings may be very similar to those of the syndrome under consideration

Although excision of thoracic aneurysms has become an accepted form of therapy during the past 8 years repair of acquired aorticopulmonary fistula has not been undertaken until recently In two recorded attempts at surgical correction, one patient survived exploration only and the other died of ventricular fibrillation during attempted removal[10, 15] In both instances, the surgeon stated that the extensive inflammatory reaction between the aneurysm and pulmonary artery made repair of the fistula technically impossible Recently, we successfully repaired an acquired aorticopulmonary fistula which we believe is the first successful case of its type

CASE REPORT

J P, a 45 year old white man, was admitted to Methodist Hospital on Nov 9, 1958, for treatment of an aortic aneurysm with suspected aortic insufficiency Nine years previously hoarseness had appeared suddenly and he had received penicillin therapy for syphilis Two years later he noted a sudden onset of weakness and paresthesia with swelling of his left arm These symptoms abated somewhat after a week, but venous distention of the extremity persisted Excessive activity resulted in recurrent swelling of this arm During the 6 months prior to admission, a dull aching substernal and lower left chest pain was noted together with progressive dyspnea Several months prior to admission he had developed a productive cough and chest pain and was treated unsuccessfully with antibiotics He was referred for surgical evaluation with a diagnosis of syphilitic thoracic aortic aneurysm with aortic insufficiency

Positive physical findings on examination included a blood pressure of 155/45 mm Hg in the right arm and 160/40 mm Hg in the left arm Pupils reacted to light and on accommodation A tracheal tug was present Prominent distention of the superficial veins of the left arm, shoulder, and left pectoral region was evident but was not accompanied by venous pulse or increased skin temperature The heart was enlarged to the left A continuous murmur with systolic accentuation localized in the left second and third interspaces was noted, and peripheral pulses were water hammer in type

Usual laboratory studies were within normal limits except for a positive serologic test for syphilis Venous pressures as measured in the upper extremities were 14 cm of water bilaterally Circulation time, arm to tongue, using Decholin was 16 seconds The electrocardiogram revealed right axis deviation and minimal right ventricular hypertrophy

Roentgenograms of the chest revealed a mass in the superior mediastinum which was considered to be an aneurysm of the aortic arch (Fig 1) An angiocardiogram confirmed the presence of the arch aneurysm and strongly supported the clinical diagnosis of aorticopulmonary artery fistula since reopacification of the pulmonary artery occurred after the contrast material had entered the aorta (Fig. 2).

Operation was performed on Nov. 11, 1958. A left anterior third interspace incision was carried across the sternum for a short distance into the right third interspace. Approximately 350 c.c. of serous fluid was found in the left hemithorax. A large saccular aneurysm, measuring 12 cm. in diameter, arose from the posterior and left side of the ascending aorta, filling the aorticopulmonary window and compressing the origin of the left pulmonary artery (Fig. 3). Although the first portion of the descending aorta was aneurysmal on its entire circumference, the dilatation in the arch was confined to the lesser curvature. A continuous thrill was palpable in the left pulmonary artery, distal to an area of aneurysmal compression. The thrill could be obliterated by compression of the area of junction between the aneurysm and the pulmonary artery. In spite of the increased venous pattern on the chest and left shoulder, the innominate vein was not compressed by the aneurysm.

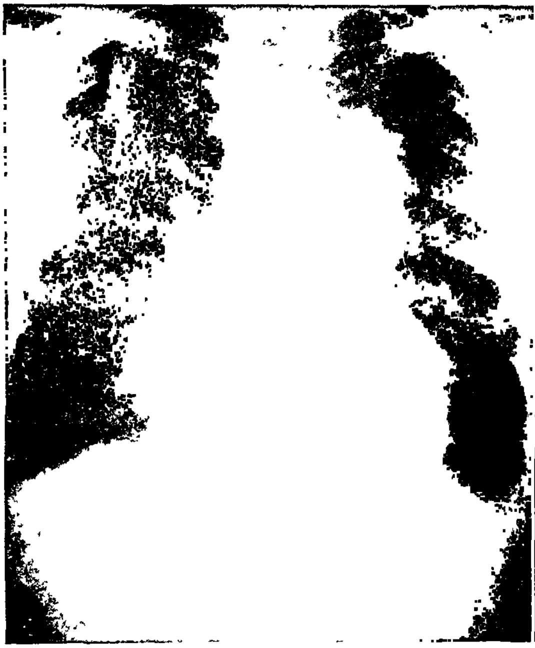

Fig. 1.—Roentgenogram of chest in 45-year-old patient showing mediastinal widening produced by an aneurysm of the transverse aortic arch encroaching upon the left pulmonary hilum.

Fig. 2.—Angioaortogram showing a fusiform aneurysm of aorta. Reopacification of the pulmonary artery is evident, suggesting the presence of an aorticopulmonary fistula.

The aorta and the left pulmonary artery were isolated at their origins by umbilical tapes. The main branches of the left pulmonary artery were isolated with heavy silk ligatures. The left subclavian artery was isolated and a tourniquet tape applied. The distal descending aorta was isolated with a tape (Fig. 3). The left phrenic nerve was preserved, but the left vagus was sacrificed since the recurrent laryngeal nerve had been compressed and destroyed by the aneurysm.

The left femoral artery was isolated and a catheter inserted for arterial perfusion. The pericardium was opened to expose the left auricular appendage, and a plastic catheter was inserted in preparation for left atrial to left femoral artery shunting using a single De Bakey roller pump (Fig. 3). The partial bypass was started using a flow of approximately 1,800 c.c. per minute, with the blood pressure in the right arm being monitored continuously.[8, 9]

A vascular clamp was *applied to the transverse aortic arch with the* blades placed somewhat obliquely across the base of the saccular aneurysm The tourniquet about the left subclavian artery was tightened to prevent back bleeding, and the descending aorta was occluded distal to the aneurysm The left pulmonary artery was occluded at its take off from the main pulmonary artery with a vascular clamp, and branches of the left pulmonary artery were occluded with tourniquet ligatures (Fig 3)

The left atrio femoral bypass was begun at a rate sufficient to maintain a mildly hypertensive state in the head and upper extremities The aorta was transected just distal to the proximal aortic clamp, and the wall of the saccular portion of the aneurysm was opened widely Large amounts of laminated thrombus were removed The fistulous communication between the sac and the pulmonary artery was readily visualized and found *to be round and smooth in outline and to measure approximately 12 mm in diameter*

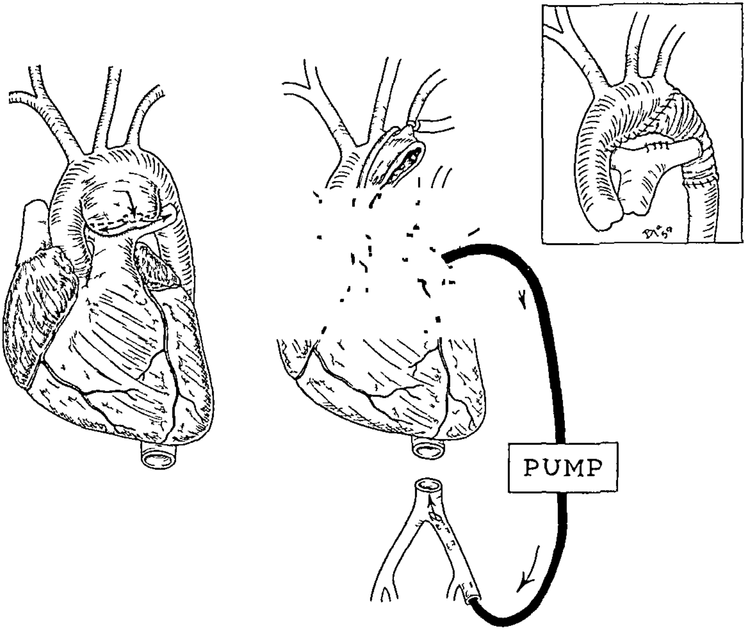

Fig 3—Drawing showing location of aneurysm of the aortic arch and fistulous communication with the left main pulmonary artery Controlled extracorporeal circulation was used to bypass the aortic arch during resection of the aneurysm and graft replacement Left main pulmonary artery was temporarily occluded proximal and distal to the fistula Inset shows completed repair using Dacron knit prosthesis

The opening in the pulmonary artery was closed with interrupted sutures of silk The remaining wall of the aneurysm was dissected from the mediastinum, and the descending aorta was transected proximal to the distal clamp A lateral aortorrhaphy was completed where the origin of the aneurysm involved the ascending aorta A knitted Dacron prosthesis, measuring approximately 12 cm in length, was sutured in place between the arch at the level of the subclavian artery and the normal appearing descending aorta following which the clamps were removed and the partial bypass discontinued The total time of aortic cross clamping and of partial bypass was 55 minutes

The postoperative course was uneventful. At the time of dismissal from the hospital 10 days later, examination revealed a normal precordium without murmurs or thrills. Aortic second sound could be heard distinctly. The blood pressure was 125/80 mm. Hg and the peripheral pulses were normal. Venous distention of the left arm disappeared. The patient was discharged on the tenth postoperative day in good condition. Examination 3 months later revealed no cardiac murmurs and a blood pressure of 140/80 mm. Hg. Roentgenograms of the chest showed a normal mediastinal configuration (Fig. 4).

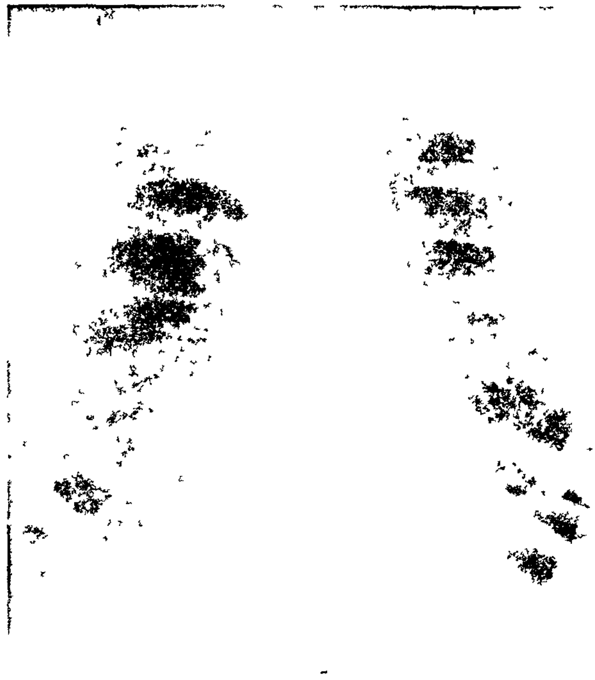

Fig. 4.—Roentgenogram of chest made 3 months after operation showing a relatively normal cardiac and mediastinal silhouette with slight elevation of left leaf of the diaphragm

COMMENT

Rupture of an aneurysm of the aortic arch into the pulmonary artery produces an acquired aorticopulmonary fistula. This lesion is similar to congenital aorticopulmonary septal defect in that no duct exists which would permit safe interruption between clamps with closure by suture. Moreover, the presence of a dense inflammatory reaction between the pulmonary artery and aorta prevents separation of the two vessels by dissection. Thus, temporary diversion of the blood stream around the area of the fistula is necessary for successful repair.[7, 8] Temporary left atrium to femoral artery bypass, using controlled extracorporeal circulation, permits safe aortic occlusion at a point close to the heart. This technique controls left ventricular strain and prevents ischemic damage to the spinal cord during the period of aortic occlusion. Temporary interruption of flow through one main pulmonary artery as used in the reported case, or partial occlusion of the pulmonary artery with a curved exclusion clamp, isolates the fistulous opening for repair If the aorticopulmonary fistula involves the ascending aorta, temporary complete cardiopulmonary bypass with the pump oxygenator should be used, similar to the method recommended for congenital aorticopulmonary defects

SUMMARY

Rupture of an aneurysm of the ascending aorta and arch is a rare complication usually leading to death within a few weeks or months Surgical correction of the resulting lesion requires temporary diversion of the blood stream around the involved segments of aorta and pulmonary artery, excision of the aneurysm, and repair of the pulmonary arterial opening In a 45 year old patient, correction of an acquired aorticopulmonary fistula, secondary to aortic aneurysm, was successful Excision of the aneurysm with restoration of aortic continuity by means of Dacron graft was performed, using a temporary extracorporeal pump oxygenator bypass

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Original Communications

DESTRUCTION OF THE SPECIALIZED CONDUCTION TISSUE IN THE LIVE CANINE HEART WITH IODINE

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IT HAS LONG been known that iodine could be used as a stain in histologic study of high glycogen containing tissue. However, there has been surprisingly little application of this method in the study of the conductive system of the heart, especially as a macroscopic method of demonstration when applied to the endocardial surface of the heart. In 1885, Marchand[7] applied an iodine solution to the endocardium of the sheep heart and noted the visualization of the conductive system. Much later, Taufic, Lewis, and Bashour[9] in 1957 applied Lugol's solution to the autopsied canine heart to demonstrate the bundle branches during the study of experimental septal defects and Uhley and associates[10] have again emphasized this technique and have applied it to a radioautographic method using radioactive iodine. These are all techniques for study of the dead heart, but recently Allen and associates[1] have suggested that iodine solution be used as a supravital staining method in clinical material during open heart surgery in order to visualize and avoid traumatic injury to the conductive system. We will present evidence to show that this is a dangerous supravital stain because of its damage to the conduction tissue.

In the canine heart, the bundle branch and Purkinje systems are very well developed and lie immediately beneath the endocardium. If looked for carefully, these structures can be seen with the naked eye as white strands of tissue

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contrasted against the background of myocardial tissue. This has been noted previously in the older literature[2, 6] and has also been noted in the beef,[3, 4, 6] sheep,[4, 6] and human[5, 8, 12] hearts. However, in the human heart this is best demonstrated with gross dissection,[5, 8, 13] and the Purkinje system cannot be seen macroscopically.

Because of its high glycogen content, the right and left bundle branch and Purkinje system of the canine heart are easily stained with iodine solution. This stain gives a dark brown to bluish color and is sharply demarcated from the adjacent myocardium. The staining reaction appears several seconds after the local application of iodine solution to the endocardial surface of the heart. The reaction works on both the fresh and the formalin-fixed heart. Fig. 1 shows the right and left bundle branches and Purkinje systems in the canine heart as they appear with this technique. In Fig. 1*A* the well-formed right main bundle branch is seen emerging from beneath the medial cusp of the tricuspid valve, where it originates in the area of the membranous septum. It passes near the muscle of Lancisi and courses down in the area of the septal band of the crista supraventricularis to the anterior papillary muscle where it bifurcates into an anterior and a posterior branch. Minor variations in the pattern of distribution of the fibers in the region of the bundle are noted in some dog hearts in that they may be more diffuse and less easily recognized as a compact bundle. Also fibers may occasionally be seen to branch off the main bundle; however, these have not been seen to end in the Purkinje network. In Fig. 1*B*, the left main bundle branch is seen emerging from the area of the membranous septum. It is very short and diffuse and almost immediately bifurcates into an anterior and a posterior branch.

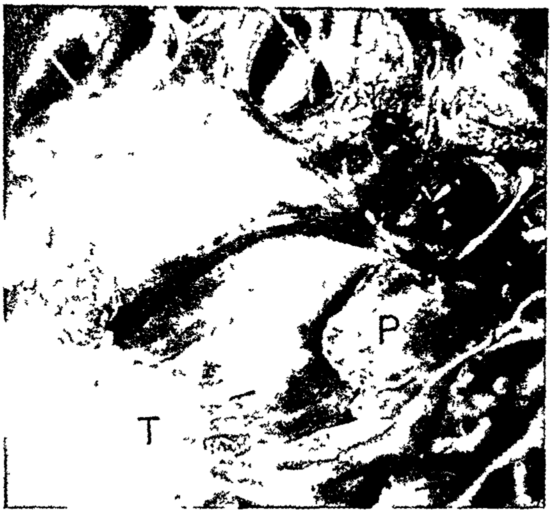

Fig. 1*A*.—Normal right bundle branch of the canine heart stained with Lugol's solution. The main bundle can be seen emerging from beneath the tricuspid valve leaflet (*T*) and bifurcating near the anterior papillary muscle (*P*) into and anterior and posterior radiation

We have not been able to visualize satisfactorily the bundle of His by this system. However, if the right main bundle is followed up to the membranous septum the common bundle lies immediately in this area.

Several years ago we became interested in this technique as a possible means of visualizing the conduction system in the living heart at the time of open heart surgery in dogs. However, we found that although Lugol's solution stained the conduction tissue well, the staining reaction caused immediate and permanent bundle branch block. Because of this observation, we abandoned the technique for this purpose, but adopted this property of destroying conduction tissue to a study of the mechanism of ventricular activation. The electrophysiologic effect of destruction of the total bundle branch and Purkinje system of the right ventricle of the dog by spraying the endocardium with Lugol's solution has been under study in the dog heart. This technique produces a block which lasts at least 9 months, the longest period of observation we have made.

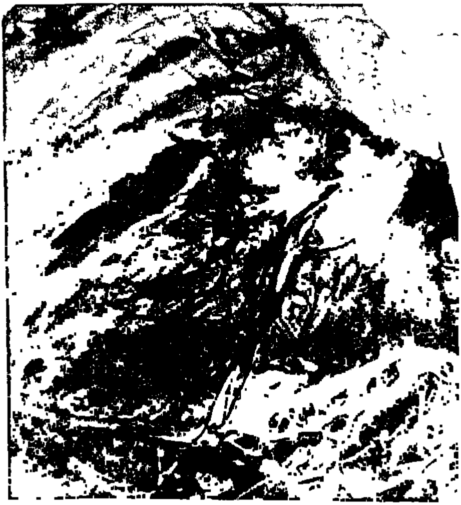

Fig 1*B*—Normal left bundle branch of the canine heart stained with Lugol's solution The left main bundle is very short and bifurcates almost immediately with an anterior and posterior radiation. The Purkinje network is well visualized.

Stimulated by the report of Allen and associates,[1] we have recently made some further observations as to the effect of iodine solutions on the right main bundle branch.

MATERIALS AND METHODS

Nine medium-sized mongrel dogs were anesthetized with intravenous sodium pentobarbital. A control 12 lead electrocardiogram was taken with a Sanborn Model 150 direct writing machine at a paper speed of 50 mm. per second. Immediately following this, at normothermia, the heart was exposed through a fourth right intercostal incision. The inflow and outflow tracts of the heart were then occluded and, through a right atrial incision, the area of the right main bundle branch on the ventricular septum was exposed by retraction of the tricuspid valve. In most instances, the main bundle branch could be identified quite well, even before staining. The bundle was stained by applying a cotton pledget dampened with the iodine solution to the bundle area for a few seconds. In all cases the bundle was stained and visualized well. The heart was then closed and the circulation restored. The total time of occlusion was from 2 to 3 minutes. The animal was allowed to recover. An electrocardiogram was taken immediately following surgery and again in 14 days, at which time the animal was sacrificed. In 2 cases, just before sacrificing the animal, the left main bundle was injured by a probe introduced into the left ventricle through the posterior myocardial wall near the septum. By this method complete right bundle branch block was proved to be present, for when left bundle branch block was added, complete heart block was noted immediately. The conduction system was examined grossly in all dogs after sacrifice with excess Nembutal. Histologic examination was also performed in 2 dogs.

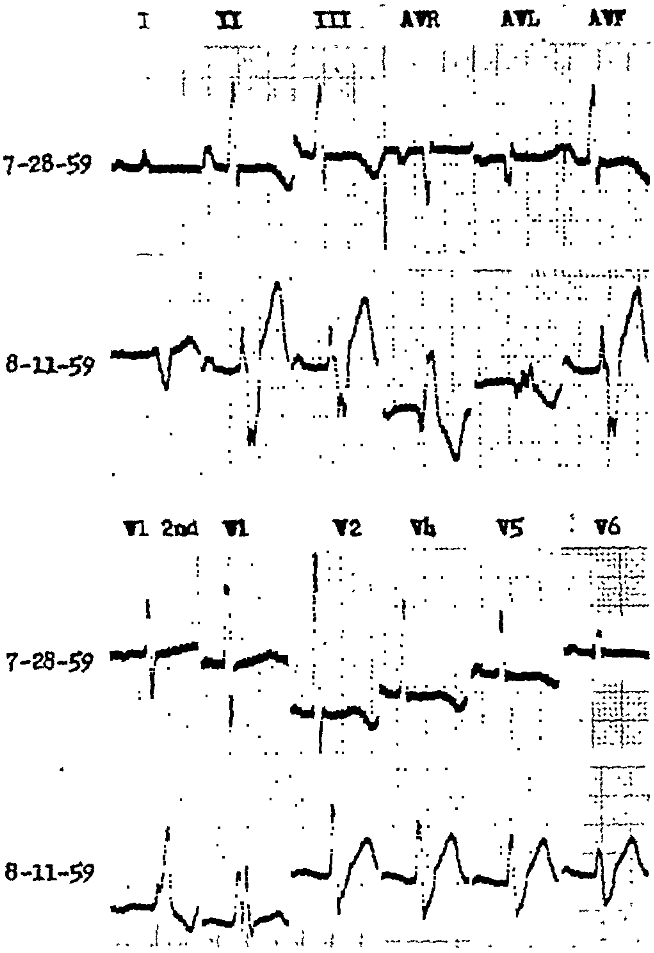

Fig. 2.—Electrocardiogram showing the typical right bundle branch block present 2 weeks following the application of iodine solution to the right bundle branch. The tracing of 7/28/59 is the control before the surgical procedure. The first chest lead is V_1 in the second interspace. V_3 is not taken because of the close proximity of V_2 and V_4 in the dog.

For the histologic work, a block was taken of the ventricular septum in the area of the bundle and serial sections were made of the entire block, staining alternate sections with the periodic acid-Schiff stain and hematoxylin and eosin. In each heart a block of the left main bundle was prepared in a similar way as a control.

In this study the iodine solutions used were: 5 per cent elemental iodine and 10 per cent KI in aqueous solution (Lugol's solution) in 6 cases, and 5 per cent elemental iodine and 10 per cent NaI in aqueous solution in 3 cases. The latter solution was the one used by Allen and his co-workers.[1] We used it in the above cases only to rule out the possibility of potassium effect with the Lugol's solution.

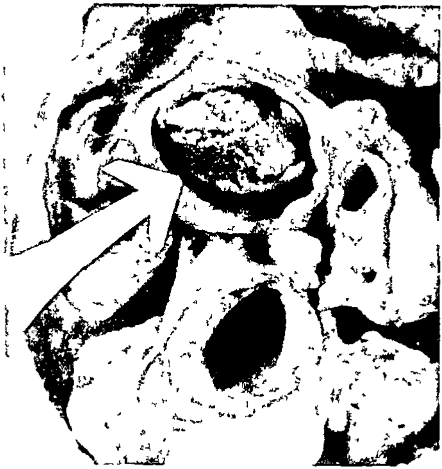

Fig. 3 —View showing almost complete occlusion of the pulmonary artery by a thrombus originating from the area of application of Lugol's solution to the septal endocardium

RESULTS

All 9 animals showed a normal control electrocardiogram There was complete right bundle branch block in the tracing immediately following surgery and in the 14-day tracing in 8 cases, while in 1 case, in which Lugol's solution was used, the block appeared to be incomplete. Fig 2 shows a typical control and final electrocardiogram. In the 2 cases in which the left main bundle branch was injured, a complete heart block developed, which proved that the block in the stained right bundle was complete

At autopsy examination, a severe tissue reaction was seen in the area of application of the iodine solution in 7 cases. In 2 cases this area was covered with a large thrombus. In 1 case (Fig. 3), the thrombus extended into the pulmonary outflow tract and proximal main pulmonary artery, causing a severe degree of obstruction of this vessel. In 2 cases the endocardial tissue reaction was not as severe and the main bundle branch could be seen as a dense white band in the area stained, which was a distinct change from its normal appearance. In all cases there was a loss of ability of the bundle to stain with Lugol's solution in the area involved. Distally the uninvolved bundle and Purkinje tissue retained this property, an observation which we have also made following cutting of the bundle.[11] There appeared to be no difference in the effect of the two solutions used.

Examination of the involved area in the 2 cases studied histologically revealed the endocardium to be inflamed and fibrotic. The conduction tissue could not be identified with either the periodic acid-Schiff or hematoxylin and eosin stain. Some sections showed organizing fibrin on the surface of the endocardium.

DISCUSSION

The use of a supravital stain to give good visualization of the conduction system during open heart surgery would be desirable in order to prevent injury to the system during the procedure. Allen and associates[1] have recently advocated the use of an iodine solution (5 per cent elemental iodine and 10 per cent NaI in aqueous solution) to accomplish this in experimental and clinical work, but our experience, as presented, clearly shows that iodine solutions are dangerous because of their deleterious effect on the conduction tissue. This is manifested as both functional and histologic change. Also, there is a severe endocardial reaction and sometimes thrombus formation in the area to which the solution is applied.

At the present time we do not know of any supravital stain which can be used on the conduction system. However, further investigation is desirable in this field because of the frequency of conduction disturbances following open heart procedures.

The bundle branches, especially the right, can be seen sufficiently well with the naked eye in the canine heart to be of use in experimental open heart procedures when injury to the system is to be avoided.

Iodine solutions give very good contrast of the bundle branches and Purkinje tissues in the autopsied canine heart for purposes of gross morphologic study.

SUMMARY

1. Iodine solutions were shown to stain selectively the bundle branch and Purkinje system of the dog heart due to the high glycogen content of these structures.

2. Iodine solutions were applied to the right bundle branch of the canine heart in 9 living animals in order to evaluate this as a supravital staining method.

3 This procedure produced bundle branch block in all cases and subsequent gross examination and histologic examination in 2 cases showed severe damage to the conduction tissue

4 The use of iodine solutions to supravitally stain conduction tissue in the human being should be thoroughly evaluated because of the readily demonstrable and permanent damage this substance produces in the conduction system of the dog

We are grateful to Dr Robert B Jennings of the Department of Pathology of Northwestern University Medical School for help in evaluating the pathologic material

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PRIMARY CARCINOMA OF THE LUNG

A Follow-Up Study Including Pulmonary Function Studies of Long-Term Survivors

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THE PURPOSE of this paper is twofold: first, to present data concerning the fate of 513 people operated upon for primary carcinoma of the lung between July 1, 1942, and Jan. 1, 1959; and, second, to call attention to the problem of cardiopulmonary illness faced by those long-term survivors who were successfully treated by pneumonectomy.

AGE

Patients varied in age from 32 to 80 years, with the highest concentration lying in the sixth decade, or more specifically, between the ages of 55 and 60 years (Table I). We have had less success in treating patients under 40 and over 70 years than those in other age groups. Of 9 patients under 40, only 2 had lesions which permitted pulmonary resection. One of these died within 3 months of the operation from metastases, and the other, although living a year and a half after surgery, has had a recurrence and is being treated by radiation therapy. Those at the other end of the age spectrum also did poorly, but for a different reason. There were 35 patients 70 or more years of age for whom we did a thoracotomy, and in this group the resectability rate of 51.4 per cent was almost as good as the over-all rate of 53.3 per cent. But the surgical mortality was considerably higher, being 8.6 per cent as compared to an over-all 2.9 per cent. There were 3 deaths, all occurring among the 9 patients who had a pneumonectomy, for a surgical mortality rate for this procedure of 33.3 per cent. There were no surgical deaths among the 16 patients explored, nor among the 10 who had lobectomy. In our experience, a deficient cardiopulmonary reserve is the greatest hazard to these older patients, and we now prefer to have complete pulmonary function studies done on them prior to surgery. We try to resect the amount of lung tissue which will provide the patient with the best over-all prognosis, taking into consideration both the cardiopulmonary function, and the nature and extent of the neoplasm.

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TABLE I. AGE DISTRIBUTION IN 513 THORACOTOMIES

AGE	LOBECTOMY	PNEUMONECTOMY	ALL RESECTIONS	EXPLORATIONS	TOTAL THORACOTOMIES
Under 40	2	0	2	7	9
40-44	4	12	16	20	36
45-49	5	28	33	29	62
50-54	8	38	46	38	84
55-59	25	47	72	62	134
60-64	19	45	64	36	100
65-69	14	18	32	21	53
70 and over	10	9	19	16	35
Totals	87	197	284	229	513

SEX

Among 513 patients were 68 (13.3 per cent) females. The proportion of females in our series increased slightly in the latter half as compared to the first half. Up to the end of 1950, 12.2 per cent of 196 patients were women, as compared to 13.9 per cent of 317 patients from the end of 1950 to the end of 1958. This increase of 1.7 per cent should not necessarily be taken to mean that there has been a similar increase in the amount of pulmonary carcinoma in women. An analysis of our data indicates that this increase is due largely to the greater number of asymptomatic, peripheral lesions being found with the more frequent use of routine chest x-ray examinations. Comparing resectability rates in the two periods, we see that in males the rate increased less than 2 per cent (from 54.7 per cent to 56.4 per cent), while the rate for females jumped over 30 per cent (from 33.3 per cent to 63.6 per cent) (Table II). Also the proportion of resections which was limited to a lobectomy, rose from about 10 per cent in the early period to about 42 per cent in the latter period. Likewise, the proportion of adenocarcinoma in the resected specimens rose from 12.8 per cent to 18.1 per cent (Table III). All of these facts, we believe, point to the conclusion that the earlier diagnosis of peripheral lesions has been of greater significance proportionately, in females than in males.

TABLE II. RESECTABILITY RATES BEFORE AND SINCE JAN. 1, 1951
SEX COMPARISONS (513 THORACOTOMIES)

	BEFORE JAN. 1, 1951			SINCE JAN. 1, 1951			TOTALS		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
Thoracotomies	172	24	196	273	44	317	445	68	513
Explorations	78	16	94	119	16	135	197	32	229
Resections	94	8	102	154	28	182	248	36	284
Resectability rate	54.7	33.3	52.0	56.4	63.6	57.4	55.7	53.0	55.4

TABLE III. PERCENTAGE ADENOCARCINOMA IN PATHOLOGY SPECIMEN
284 RESECTIONS: 248 MALES—36 FEMALES

	BEFORE JAN. 1, 1951	SINCE JAN. 1, 1951	TOTALS
Males	11—11.8%	19—12.3%	30—12.1%
Females	2—25 %	14—50 %	16—44.4%
Totals	13—12.8%	33—18.1%	46—16.2%

The early surgical results are shown in Table IV. Among the 513 patients having thoracotomy, there were fifteen deaths within the first 2 weeks, for a surgical mortality rate of 2.9 per cent. Only one death in 229 operations (0.4 per cent) occurred following exploration. Likewise, following 87 lobectomies, there was only one death, for a surgical mortality rate of 1.1 per cent. The highest rate occurred in those patients having pneumonectomy, where there were 13 deaths in 197 operations, for a mortality rate of 6.6 per cent. This gives an over-all mortality rate among 284 patients having pulmonary resection of slightly under 5 per cent (14 deaths). Three of these 14 deaths occurred in poor-risk patients over 70 years of age who had pneumonectomy.

TABLE IV. EARLY SURGICAL RESULTS (513 THORACOTOMIES)

	MALES	FEMALES	TOTAL
Number of thoracotomies	445	68	513
Surgical mortality	15	0	15—2.9%
Number of explorations	197	32	229
Surgical mortality	1	0	1—0.4%
Number of resections	248	36	284
Surgical mortality	14	0	14—4.9%
Number of lobectomies	65	22	87
Surgical mortality	1	0	1—1.1+%
Number of pneumonectomies	183	14	197
Surgical mortality	13	0	13—6.6%

LATE RESULTS OF SURGERY

For about one half of our patients who had pulmonary resection, the operation had little influence in prolonging their lives (Table V). These, obviously, were the patients in whom the carcinoma had extended beyond the lung or had metastasized by way of the blood or lymph stream prior to the time of surgery. In a few of them, there was suggestive evidence of metastasis or extension at the time of surgery and the prognosis was thought to be bad. But in most of them there was no apparent evidence of metastasis at the time of resection. Approximately 50 per cent of those having a resection died within the first year after surgery, which compares with a 95 per cent death rate within the first year after exploration for a group followed earlier.[1] After the first year, the death rate for carcinoma rapidly diminished, and by the third postoperative year, about 90 per cent of those who were to die of carcinoma had already done so (Fig. 1).

TABLE V. RESECTION SURGERY: LATE RESULTS

YEARS IN WHICH RESECTED	1942-1957	1942-1955	1942-1953	1942-1948
Length of time observed	1 year	3 years	5 years	10 years
Number of patients	249	202	162	64
Number dead or lost	123	139	126	52
Per cent dead or lost	49.4	71.8	80.9	81.2
Number known alive	126	57	31	12
Per cent known alive	50.6	28.2	19.1	18.8

In previous publications,[1, 2] we presented follow-up data for a small group of patients who had been treated by lobectomy. Lobectomy had been done in these patients as an operation of choice, the criteria for the selection being (1) a peripheral lesion well removed from fissures, pleural surface, and point of bronchial transection, and (2) in which the mediastinal and hilar lymph nodes did not appear to be involved in a metastatic process. This small group of patients had a 3-year survival rate of 75 per cent. Since that time, we have performed lobectomy in some patients as a palliative procedure, and in others as a second choice because of poor cardiopulmonary reserve. This has, of necessity, lowered the long term survival rate for this operation. At the present time, the 3 year survival rate for 52 patients having lobectomy is 51.9 per cent as compared with 20 per cent for 150 patients having pneumonectomy (Fig. 2).

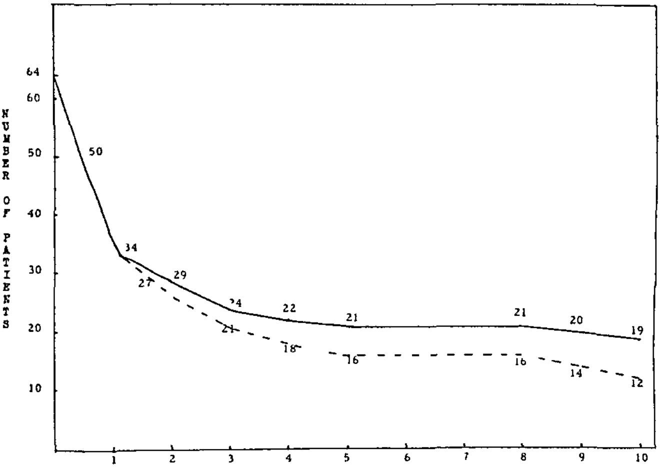

Fig. 1.—Ten year follow up after resection on 64 patients—63 pneumonectomies and 1 lobectomy. *Dotted line*, number of survivors. *Solid line*, number of carcinoma survivors.

Ten Year Survival.—In this series of 513 patients, are 63 who had a pneumonectomy more than 10 years ago. Thirty of these 63 died of carcinoma within the first year after surgery. In the next 9 years, 22 more died, but of the 22, 7, or about one third, died of causes other than carcinoma. Considering the age of the people involved, this is not surprising, nor, perhaps, is it surprising that 5 of these deaths were reported as of cardiac origin. We have wondered, however, to what extent and in what way the loss of one lung may have contributed to their so called "cardiac" deaths. Were they not in reality cardiopulmonary deaths? And if so, could something perhaps have been done to prolong their lives? It has been suggested that the distention of the remaining lung following pneumonectomy produces pulmonary emphysema, which in turn reduces the cardiorespiratory function. It has been further suggested that thoracoplasty should be done in order to reduce distention in the remaining lung.

In order to study this problem, we decided to bring in the 11 patients who are still alive 10 or more years after pneumonectomy. The length of their survival varies between 10 and 16 years, with the average being 12.7 years. With one exception, the 11 patients are all leading satisfactory lives. They are either working, or are exerting an equivalent amount of physical activity. The one exception is F. O. H., who, strangely enough, is the oldest in respect to survival time (16 years), but the youngest in actual age. At the time of surgery, he was 42 years old. Within the past 2 years, he has had two episodes of right heart failure, and was almost totally incapacitated at the time of the study. He has recently died of right heart failure.

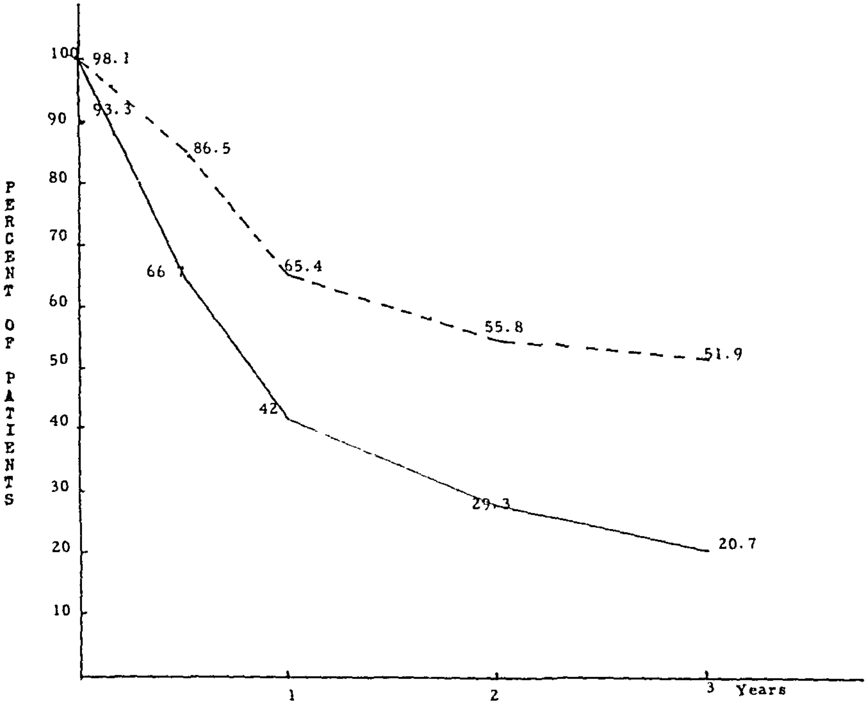

Fig. 2.—Three-year follow-up after resection. *Dotted line:* patients having lobectomy. *Solid line:* patients having pneumonectomy.

We were able to do complete pulmonary function studies on 9 of the 11 patients (Table VI).

TABLE VI. PATIENTS STUDIED 10 OR MORE YEARS AFTER PNEUMONECTOMY

PATIENT	SIDE	AGE	YEARS SINCE SURGERY
1. F. O. H.	Left	57	16
2. H. J. H.	Right	68	10
3. H. B.	Right	65	12
4. H. H.	Right	60	13
5. L. Z.	Left	64	15
6. R. B. (Mrs.)	Right	57	10
7. J. C.	Left	66	12
8. J. O. R.	Left	65	12
9. R. B.	Right	65	14

PULMONARY FUNCTION STUDIES

Methods—The lung volume measurements consisted of spirograms on the 13 5 liter respirometer before and after bronchodilator drugs such as Vaponefrin and Isuprel The measurements from the spirogram included total vital capacity, timed vital capacity for 3 seconds, and the maximal breathing capacity The shape of the spirogram tracing was also of significance The residual air was measured and checked both by the oxygen open circuit[3] and the helium closed circuit methods[4] The alveolar nitrogen was obtained on oxygen breathing after the end tidal nitrogen was reduced to 1 per cent as monitored by the *nitrogen meter* *The oxygen content, oxygen capacity,* CO_2 *content and* pH were obtained on resting and exercise samples of the arterial blood, employing the manometric Van Slyke apparatus The arterial blood oxygen saturation was determined both from oxygen content and capacity measurements and by employing the Waters double scale cuvette oximeter for blood The oxygen capacity was checked both by the flask and Van Slyke methods Arterial blood samples were obtained at rest and with exercise, on air and graded levels of high oxygen breathing (33 8 per cent and 100 per cent), and with intermittent positive pressure breathing on compressed air The subject was allowed to breathe the 33 8 per cent oxygen for 8 to 10 minutes before the exercise was started The pulmonary ventilation measurements were obtained from gas analysis, using the Scholander apparatus, of the expired air collected in a Tissot gasometer The effective tidal air was calculated from the expired pCO_2 and the arterial pCO_2, the latter measurement by the direct bubble tension technique The carbon monoxide diffusion capacity was measured by the steady state method described by Filley and his co workers[6]

Results—The lung volume measurements reveal that the total vital capacity in all patients except one was 44 per cent or greater, of the predicted normal for both lungs (Table VII) The normal division of function in the lung is 55 per cent for the right and 45 per cent for the left The timed vital capacity for 3 seconds was significantly decreased as compared to the total vital capacity in 7 cases There was a marked decrease in the maximal breathing capacity in 5 cases with a moderate decrease in the other 4, but a significant degree of bronchospasm was observed in all

The absolute volume of the residual air was markedly increased in Case 1, slightly increased in Case 3, and decreased below the predicted normal in all of the others In Cases 5 and 6, the residual air was decreased almost in proportion to the vital capacity The total lung capacity varied from 47 to 68 per cent of normal predicted The ratio of the residual air to total lung capacity was markedly increased in Case 1, moderately increased in Cases 3, 7, and 9, slightly increased in Case 8, and normal in the other 4 However, the helium equilibration time, the nitrogen washout curves (Fig 3), the alveolar nitrogen per cent after oxygen breathing, and the absolute volume of the residual air indicates that emphysema was not present in a significant degree in 8 of the 9 patients A severe degree of emphysema was present in 1 patient or less (Fig. 3). In 4 patients, the nitrogen washout was very slightly prolonged beyond the 5-minute time interval, but was significantly prolonged in Case 1 only; and even in this patient the prolongation was not as marked as seen in patients with comparable severe emphysema. A composite graph is shown in Fig. 3 of 36 cases, all with severe emphysema and residual ratios of 50 to 60 per cent of total lung capacity.

The arterial blood studies revealed that only the patient with emphysema (Case 1) had a severe degree of arterial blood oxygen unsaturation at rest (below 90 per cent). A slight to moderate degree of arterial unsaturation was present in the others at rest. With step-up exercises, 1 patient (Case 2) with severe bronchospasm developed a severe degree of arterial blood oxygen unsaturation and a marked drop below the resting level. In 5 patients, there was no significant change with exercise, and in the other 3, a slight drop in 1 and a moderate drop in 2. The arterial saturation was significantly increased in all patients at rest on intermittent positive pressure breathing on compressed air only, indicating the presence of poorly ventilated alveoli as responsible

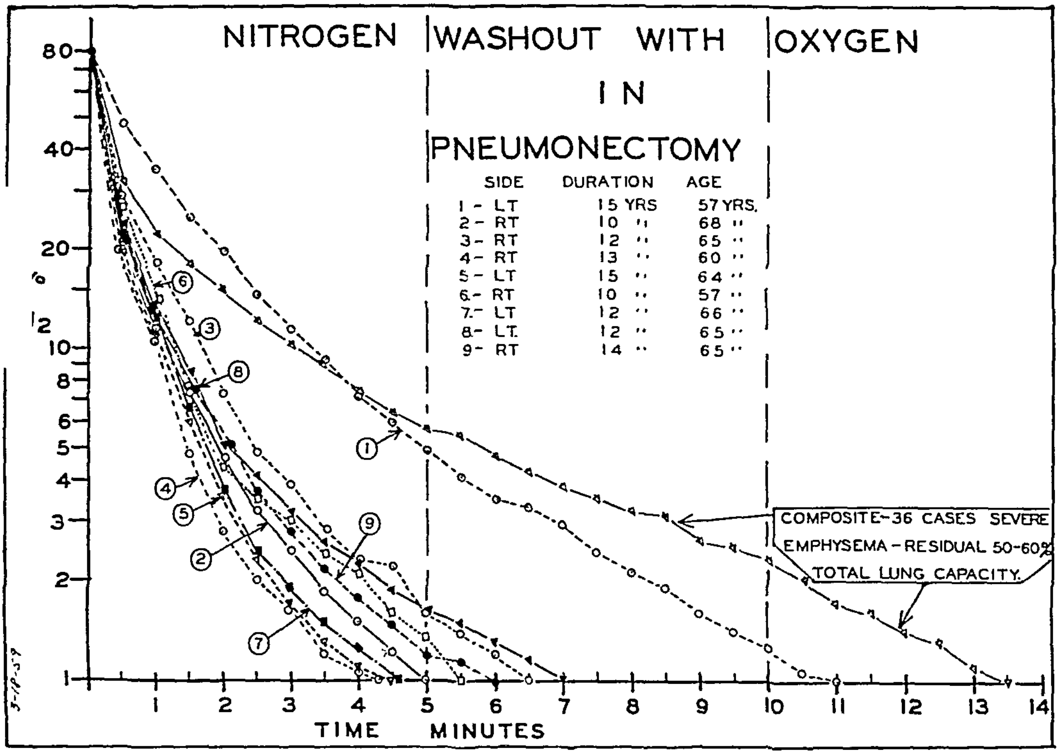

Fig. 3.—Nitrogen washout with oxygen breathing with the Waters nitrogen meter in 9 cases of pneumonectomy and a composite curve of 36 cases of severe emphysema (all with a residual ratio to total lung capacity between 50 and 60 per cent). The nitrogen concentration as per cent in the expired air is plotted on the ordinate against time at 30-second intervals on the abscissae using semilog paper. The nitrogen washout curve was normal for Cases 2, 4, 5, and 7. In Cases 3, 6, 8, and 9, the nitrogen washout curve was very slightly prolonged beyond 5 minutes to an end tidal of 1 per cent and indicates the absence of a significant degree of impairment in air distribution. The nitrogen washout curve for Case 1 was significantly prolonged and characteristic of the type seen in severe emphysema. However, the nitrogen washout for Case 1 was significantly better than the composite curve for severe emphysema of a comparable degree as based on the residual per cent of total lung capacity.

for part of the unsaturation However, part of the hypoxia was due to the perfusion of blood through nonventilated areas with exercise, as the saturation did not increase to 97 per cent or more in all cases on a 33 8 per cent oxygen breathing with an increase in the inspired pO_2 over 90 mm Hg above that of air breathing[7]

The carbon monoxide diffusion capacity measurement using the steady state method of Filley and his associates was low at rest in all cases except 1, and with exercise in all cases except 3 The lowest values with exercise were present in the patient with emphysema and the patient with severe bronchospasm (Cases 1 and 2)

The carbon dioxide content of the arterial blood was very slightly elevated above the average normal of 48 5 volume per cent, both at rest and with exercise The arterial pH was normal both at rest and with exercise Direct tension measurements of the arterial blood at rest reveal fairly normal values except for the emphysema patient, where the pCO_2 was increased and the pO_2 decreased The oxygen transport across the lung was also fairly normal as measured by the inspired alveolar pO_2 difference and the alveolar arterial pO_2 difference, except for the patient with emphysema (Case 1), and the increased alveolar arterial pO_2 difference in Case 2 (severe bronchospasm)

The minute ventilation was essentially normal both at rest and with exercise The resting oxygen uptake was decreased slightly in all patients except 2, as shown by the direct measurement of the basal metabolic rate on air breathing The exercise oxygen uptake was very markedly decreased in the patient with emphysema (266 ml per min per sq M, BSA, normal 500 to 600) A marked decrease in exercise oxygen uptake was present in 5 patients and a moderate decrease in the other 3 The decrease in the exercise oxygen uptake is quite significant in this series of cases as it indicates the inability to increase the pulmonary blood flow corresponding to the degree of exercise given, and indirectly indicates increased pulmonary vascular resistance and the probable presence of cor pulmonale There is a slight to moderate degree of impairment in the lung ventilation efficiency, as measured by the per cent of oxygen extracted both at rest and with exercise The effective tidal air based on the expired pCO_2 and the arterial pCO_2 was significantly decreased in all patients, being below the normal predicted value of 75 per cent The calculated physiological dead space was markedly increased in 2 patients while at rest

The data on these 9 patients with pneumonectomy indicate that, over all, cor pulmonale is a more significant factor than emphysema in producing disability Except in one instance, emphysema was not a significant factor in these studies of lung function Air distribution in the lung was normal for 4 patients, very slightly impaired in 4, and severely impaired in the patient with emphysema The impairment in the arterial blood oxygen saturation was due to poorly ventilated alveoli and the perfusion of blood through nonventilated alveoli, especially with exercise Bronchospasm and fibrosis appear to be primarily responsible for the hypoxia The exercise oxygen uptake was significantly decreased in all cases, and to a marked degree in all cases except 3, where the decrease was of a moderate degree. These measurements indicate the inability to expand the pulmonary vascular bed in a normal manner with exercise and the presence of increased pulmonary vascular resistance. The changes in pulmonary vascular resistance cannot be explained on the basis of pulmonary emphysema in 8 of the 9 cases. Since the rationale of a prophylactic thoracoplasty as performed shortly after a pneumonectomy is to prevent the development of emphysema, it would appear that in these patients such a procedure would have been without value, as significant emphysema is not present 10 to 15 years later. Furthermore, the deformity of a thoracoplasty could have impaired still more the ventilatory and circulatory defects which exist at the present time.[8]

DISCUSSION

The technique of pulmonary resection for carcinoma of the lung is well and long established, and the surgical risk of the operative procedure per se is satisfactorily low. But that is not equally true of the effects of resection pon the patient's physiology. His survival, both short and long time, will epend not only upon the success of the surgeon in resecting all of the neoplastic disease, but also upon the degree of disturbance in his cardiopulmonary ystem produced by the resection. Since death is the ultimate fate of all mankind, our aim in treating a patient with carcinoma is not only to alleviate uffering, but also to prolong life to the best of our ability.

Our success in arresting the fatal course of a neoplastic process by surgical extirpation certainly leaves a great deal to be desired. In only about one half of those in whom we think we have performed a successful resection will one year of postsurgical life be realized, and only about one fourth of them will survive for a period of 5 years. In our experience, this appears to be true regardless of whether the extent of the resection is a lobe or the entire lung, so long as all visible neoplastic tissue is resected, together with a safe margin separating the resected from the uninvolved tissue. Such being the case, we feel hardly justified in performing a complete pneumonectomy in every patient, regardless of the state of his cardiopulmonary physiology. Any further improvement in salvage rates, so far as surgical treatment of carcinoma is concerned, would appear to depend primarily upon earlier diagnosis and treatment. This is not true in regard to improvement in the survival rates of patients who have had successful resection. Here, there are two avenues for improvement. The first has to do with a better selection of the surgical procedure to fit the patient, and the second deals with reducing factors which are responsible for cardiopulmonary failure following resection. The means to the first are pretty well at hand—that is, the preoperative use of pulmonary function studies and other tests by which physiological status may be evaluated. The attainment of the second objective will depend largely upon the accumulation of additional data.

We think that these studies on this small group of patients have been informative, and that additional fields for investigation are quite clearly indicated. All 9 patients were, at the time of the examination, suffering from some degree of cardiopulmonary incapacity. In only 1 case was this due chiefly to pulmonary emphysema. In the other 8 cases the disability was obviously due to other factors. It is true that the appearance of their x-ray films would suggest that distention of the remaining lung is a factor (see Fig. 4 for a representative case). But the pulmonary function studies did not demonstrate evidence of pulmonary distention in any patient. Surprisingly enough, the one in whom the studies came closest to indicating pulmonary distention was the only patient who had had a postresection thoracoplasty. His roentgenogram (Fig. 5) showed the mediastinum to be pretty much in the midline. There was only 1 patient who showed a significant degree of pulmonary emphysema (Fig. 6). But since none of the others did, we feel that it is reasonable to assume that his emphysema was a concomitant, rather than a consequential, complication of the resection. Evidence of pulmonary fibrosis was, on the other hand, apparent in all of the patients studied, and does therefore appear to be a related complication. Of equal importance was the finding in all cases of evidence of the presence of an increased resistance in the pulmonary vascular bed. It cannot be said whether this increased resistance is due to a loss of expansibility produced by perivascular fibrosis, or to pulmonary arteriosclerosis resulting from the long-continued increased blood flow. It may, of course, be due to both factors. Although we did not perform right heart catheterization as part of the pulmonary function studies, it is assumed from the data collected that pulmonary hypertension was present. This would be in keeping with reports published by Adams and his co-workers,[9] who found evidence of pulmonary hypertension and cor pulmonale in their postpneumonectomy patients.

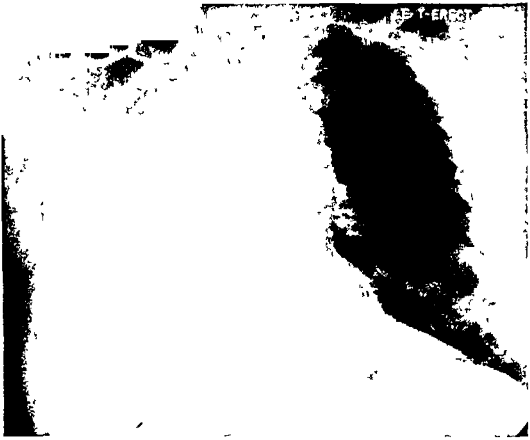

Fig 4—H H—13 years after right pneumonectomy

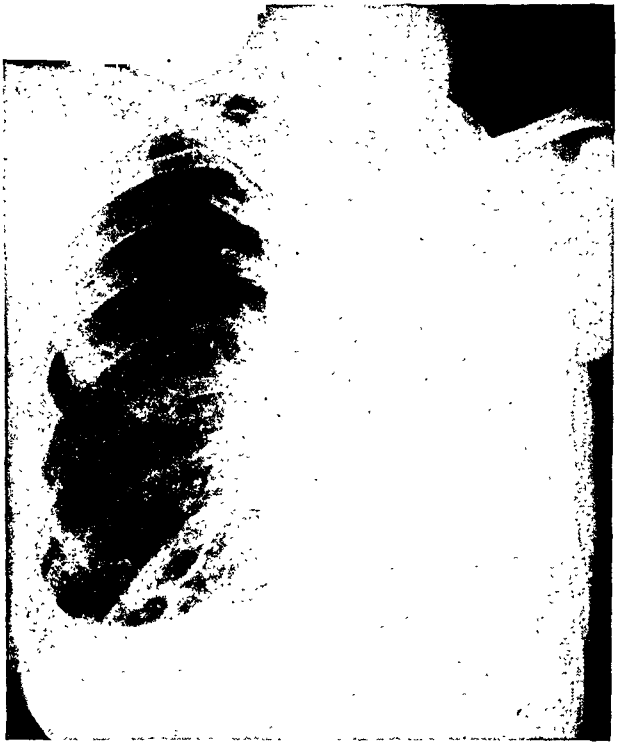

Fig. 5.—J. C.—12 years after left pneumonectomy.

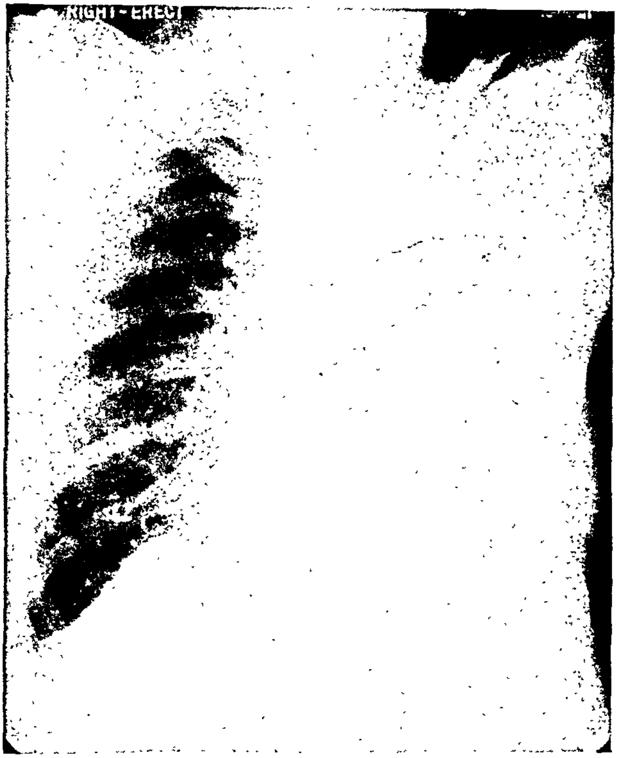

Fig. 6.—F. O. H.—16 years after left pneumonectomy.

And what has caused pulmonary fibrosis in these patients? Is it related to pulmonary arteriosclerosis, or is it due to the increased flow of air in and out of the remaining lung for a long period of time? Certainly, additional studies are needed before we can answer any of these questions. It would appear to be worth while in the future to include pulmonary function determinations in the presurgical work-up of more patients. Either then, or at the time of surgery, pulmonary arterial pressures should be recorded for future reference. Pulmonary function studies should then be repeated in those who survive resection for 1 year, and at intervals of 1 or 2 years thereafter. Information obtained from such studies might very well help us to prolong the lives of those who have had successful pulmonary resection for carcinoma. In the meantime, treatment of our long-term survivors should be directed toward relieving their bronchospasm and reducing the daily strain upon the right heart by limiting their physical activity.

SUMMARY

Thoracotomy was performed because of primary carcinoma of the lung on 513 private patients between July 1, 1942, and Jan. 1, 1959. The surgical mortality rate was 2.9 per cent. In 229 cases, exploration only was carried out, with a mortality of 0.4 per cent. In the remaining 284 patients, lobectomy was performed in 87 with one death (mortality of 1.1 per cent), and pneumonectomy in 197 with thirteen deaths (mortality 6.6 per cent), for an over-all resection mortality rate of a little under 5 per cent. Three of the 13 deaths following pneumonectomy were in patients over 70 years of age. An increased use in the community of routine chest x-ray examinations during the last one half of the period of study has resulted in bringing in more people with peripheral, asymptomatic lesions, and in an increase in the percentage of adenocarcinoma in the resected specimen from 12.8 to 18.1 per cent. Probably for the same reason, there has been an increase in the proportion of females from 12.2 to 13.9 per cent. Twenty per cent of 150 patients having pneumonectomy survived for 3 years or more. Of 52 patients having lobectomy, 51.9 per cent survived for 3 years or more. Especially interesting to us have been 63 patients who had pneumonectomy 10 or more years ago. Of the 33 who survived 1 year, 15 died later of carcinoma, but 7 died of causes other than carcinoma, and the majority of these deaths was attributed to cardiac failure. This fact prompted us to study the cardiopulmonary function of the 11 survivors. Of the 11, we were able to do complete pulmonary function studies on 9. Although all but 1 of these were living satisfactory lives and either working or reasonably active, they all suffered from some degree of cardiopulmonary disability. The function studies indicated that, except for 1 case, pulmonary emphysema was not a significant problem; nor was distention of the remaining lung. The abnormalities which appeared to us to be responsible for their disability are pulmonary fibrosis, bronchospasm, and increased resistance of the pulmonary vascular bed. Although not proved by cardiac catheterization, pulmonary hypertension was inferred to exist. Right heart

disease appears to be the greatest problem faced by these long-term survivors of pneumonectomy. Additional studies directed toward determining causative factors are needed.

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LUNG PERFUSION WITH CHEMOTHERAPEUTIC AGENTS

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THE EXPERIENCE gained in the application of mechanical extracorporeal circulation methods in cardiac bypass and in hemodialysis lends itself well to administering carcinolytic agents. The perfusion of an organ isolated from its arterial and venous supply has the immediate appeal of restricting a toxic agent to that organ.

Chemotherapy in treating cancer is a relatively new and promising field. It has been limited by unfortunate side effects particularly seen in hemopoietic depression and gastrointestinal disorder. In general, these agents have a short life as far as activity once mixed with whole blood. Therefore, long perfusion periods are not necessary to deliver a maximum dose of any agent or agents.

With these principles in mind, a safe and simple technique for perfusing the lung in dogs has been developed. Such a method permits the maximum tolerated dose of a given agent to be determined for the lung tissue. It also furnishes information as to the maximum dose of the agent in terms of function of survival, once the contralateral lung is removed.

It is hoped that such a method will prove useful as a form of bioassay of existing chemotherapeutic agents as well as those to be developed in the future.

Clinical application of this technique is under study. If it proves to be practical, the surgeon may have a method of palliation to offer those patients with inoperable lung cancer at the time of thoracotomy.

METHOD

Operation.—Dogs weighing forty pounds or more were anesthetized with intravenous Pentothal sodium and placed on intermittent positive pressure oxygen flow administered through an endotracheal tube with inflated cuff. A left fifth rib thoracotomy was performed and the left pulmonary artery and veins were exposed by incising the pericardium at its reflection over these vessels. The left pulmonary artery was mobilized and occluded by a double loop of umbilical tape just lateral to the conus. The left half of the atrium was then freed from the trachea and posterior mediastinal space to allow a Satinsky clamp to occlude the atrial chamber lateral to the anterior descending coronary vessels.

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After a second umbilical tape was fixed around the pulmonary veins to control blood loss, a 15 mm. incision was made in the lateral wall of the auricle just above the origin of the inferior pulmonary vein. Using No. 1 braided silk suture on an atraumatic round needle, a purse-string ligature was placed in the margin of the cardiotomy. This suture served to fix a Lucite button in the wall of the atrial chamber. The button (Fig. 1) was designed in the laboratory for the experiment and, once in this position, has never obstructed the outflow of venous blood to the perfusion circuit.

The pulmonary artery was then cannulated by a flanged, curved polyethylene tubing (PE 980).

No attempt was made to occlude the bronchial circulation.

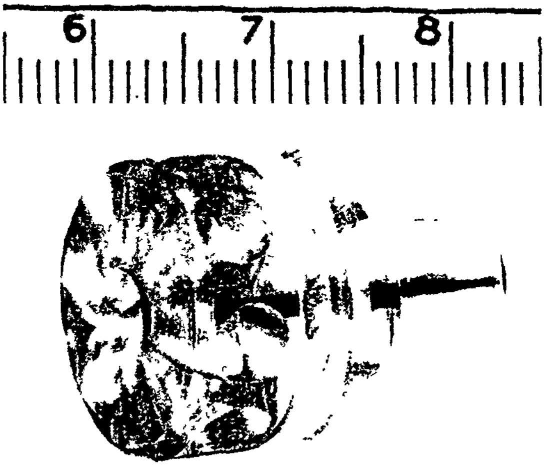

Fig. 1.—Enlargement of Lucite "button" designed to collect blood from the left half of the atrial chamber. The grooved central portion anchors the "purse-string" sutured cardiotomy in position. Ratio of collecting inlet diameter to outlet diameter is 9 to 1. The tip of the "button" fits a 0.5 cm. I.D. Tygon tubing.

The outflow and inflow cannulae were allowed to fill with blood from the isolated left lung. Clotting was prevented by administering intravenous heparin to the animal prior to the cannulation. A dose of 0.8 mg. per kilogram body weight was used. These cannulae were then connected to the perfusion apparatus.

After perfusion, the cardiotomy was closed with a running suture of 4-0 silk and the Satinsky clamp was released after precautions were taken to prevent air emboli. The pulmonary artery incision was closed with 5-0 silk in a transverse fashion which prevented stenosis. The chest wall was then closed over a water-seal drain.

Perfusion Technique.—The perfusion apparatus consisted of a Sigmamotor pump, a 500 ml. siliconized collecting bottle, and Tygon tubing connections to the cannulae. Just proximal to the pumping point, a right angle connection was attached to a 50 ml. titrating burette which was equipped with a stopcock and Murphy drip chamber (Fig. 2).

The entire perfusion circuit was sealed so that the pump not only propelled blood through the pulmonary artery but created a balanced negative pressure in the reservoir which aided the outflow of blood from the pulmonary veins. Two hundred and fifty milliliters of whole blood, anticoagulated with heparin, was used to prime the perfusion circuit. The priming level remained constant throughout the perfusion period.

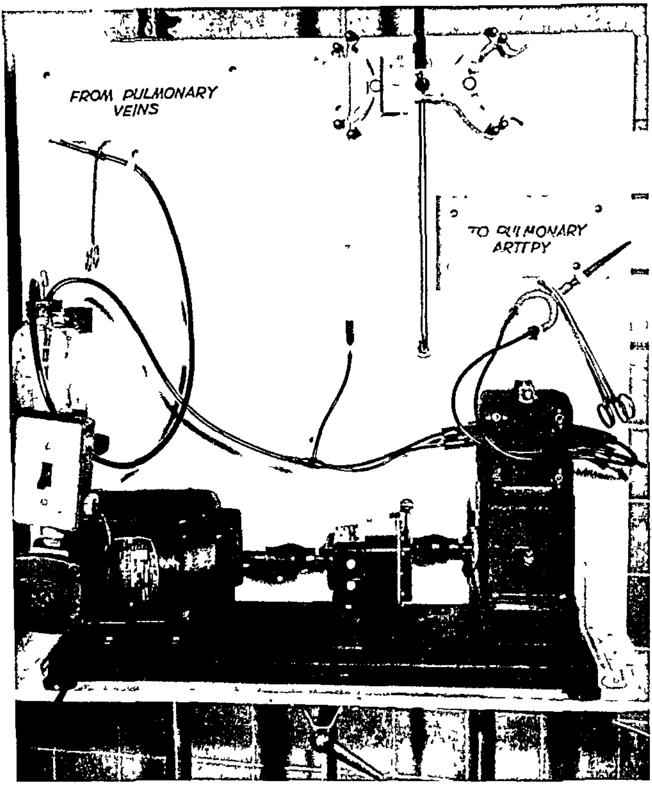

Fig 2—Vertical adjusting rack mounting Sigmamotor pump, collecting bottle, burette for chemotherapeutic agent, and disposable Tygon connecting tubes for perfusing the left lung.

The titrating burette contained a freshly prepared solution of nitrogen mustard* in isotonic saline which was added drop by drop to the circuit after the perfusion was begun.

The flow rate of the recirculating blood was maintained at 175 ml. per minute. The nitrogen mustard solution was added over the first 2 to 3 minutes of a 15-minute perfusion time.

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*Mustargen (methyl-bis-[beta-chlorethyl]-amine hydrochloride), Merck & Co, Inc., Philadelphia, Pa.

No attempt was made to wash out the perfusion blood from the pulmonary vascular bed in this series. This was based on the observation made by Creech, Krementz, Ryan, and Winblad[1] that nitrogen mustard becomes inactive or fixed in whole blood in approximately 8 minutes.

Dose of Nitrogen Mustard.—In the first 10 perfusions, random dosages of 0.2 to 0.7 mg. per kilogram of total body weight were used. There were no survivals in dosages above 0.4 mg. per kilogram. The remaining twenty-three perfusions therefore were made using this amount of nitrogen mustard.

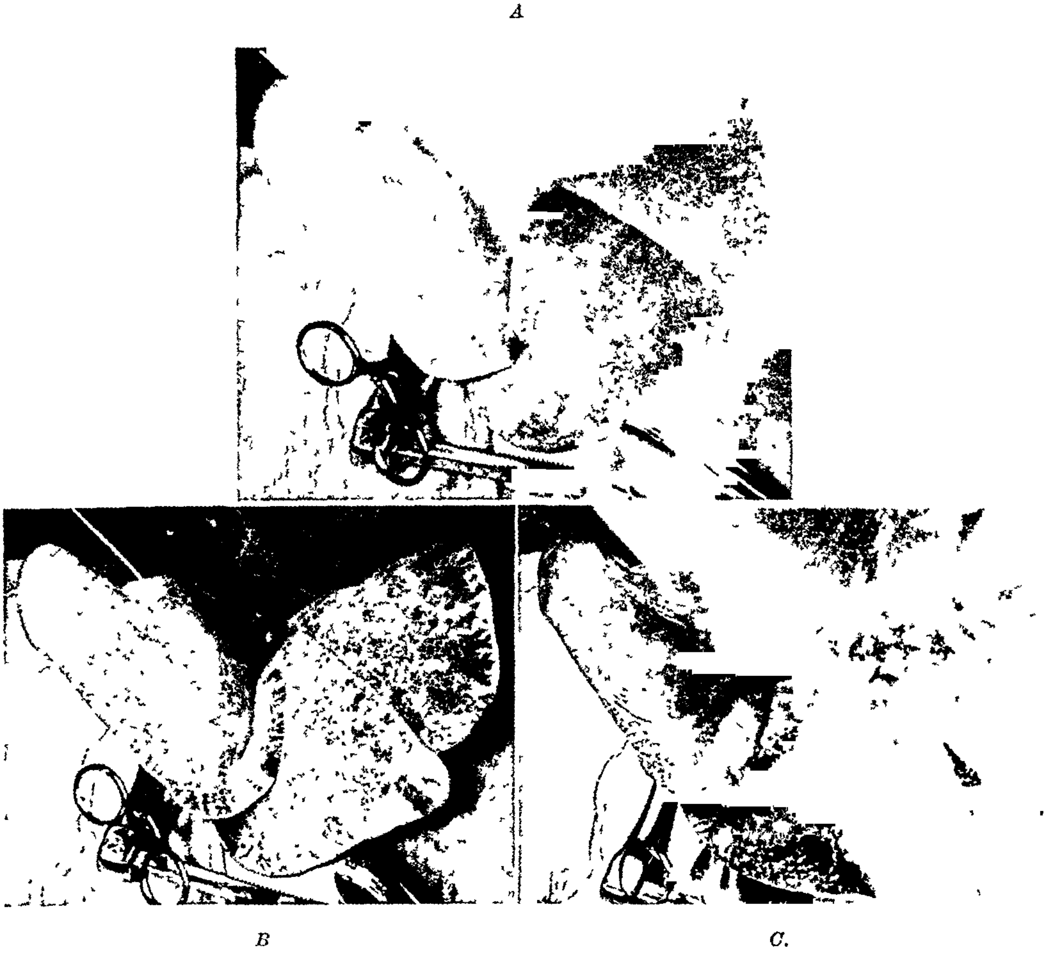


Fig. 3.—Illustration of the dispersion of methylene blue dye in the whole blood perfusion of animal's left lung. *A*, Before injection of dye. *B*, Three minutes after instillation of dye in perfusate. *C*, Five minutes after instillation of dye in perfusate.

The Perfusate.—Whole blood was selected to minimize pulmonary edema. Saline and plasma were tried but found to be unsatisfactory because a crepitant wet lung developed rapidly, early in the perfusion.

Radioactive chrome-tagged red blood cells were added to the perfusate during initial studies to determine the escape of the perfusate to the host circulation. In five separate perfusions, no trace of the radioactive element could be found in peripheral blood samples taken at the completion of the experiments.

The rapid and even distribution of the perfusate throughout the lung tissue was confirmed by infusion of methylene blue dye Within 5 seconds after the column of dye was seen to enter the pulmonary artery, all divisions of each lobe were seen to be uniformly stained with the dye (Fig 3)

The rate of flow of the perfusate was another important factor in preventing pulmonary edema Initially, rates of 300 ml per minute were found to cause a high incidence of edema, congestion, and bronchial effusion These complications were controlled by reducing the rate of flow to 175 ml per minute

Oxygenation of the perfusate was supplied by the tracheobronchial oxygen flow from the resuscitator This eliminated the need for an oxygenator in the perfusion circuit

RESULTS

Results of this experiment fall into three categories (1) survival of the animal using the maximum tolerated dose of nitrogen mustard, (2) evidence of systemic toxic effect based on periodic red blood cell and white blood cell counts, and (3) histologic evaluation of the perfused lung tissue at intervals following perfusion

In a series of 23 consecutive animals all perfused with 0 4 mg nitrogen mustard per kilogram total body weight at 175 ml per minute, there were 10 survivors Of the remaining 13 animals, 2 died of acute pulmonary edema, one of cardiac arrest, one from pneumothorax, one from hemorrhage at the cardiotomy site, 3 from pneumonitis, and 5 from distemper

The 10 validated survivors are all well and the effect of the nitrogen mustard on the peripheral blood count is tabulated in Figs 4 and 5 Three of the 10 animals had an appreciable depression of the red blood cells and only one showed a leukopenia It is possible that distemper again played a role as the anemia was not uniform throughout the group

Histologic study of perfused lung tissue is not yet complete but in this preliminary series there are specimens covering 1 to 35 days following the operation In general, the histologic changes are similar to acute pneumonitis with resolution in that there is a sequence of vascular effusion and hemorrhage, cell necrosis, monocytic infiltration, and later fibrosis

DISCUSSION

The ability to perfuse one lung without interrupting the general circulation is a distinct advantage of this experiment In 1953, we found the dog s lung can be isolated from its pulmonary and bronchial blood supply for 30 minutes and survive contralateral pneumonectomy The present experiment indicates one lung can be isolated from the host and perfused with a dose of nitrogen mustard, 175 to 200 times that which can be given intravenously The capacity of lung tissue to withstand such a chemical insult offers a new technique for administering chemotherapeutic agents This method is an improvement on the intravenous and intra arterial routes in that a higher concentration of the agent may be fixed in the lung tissue without disturbing the bone marrow

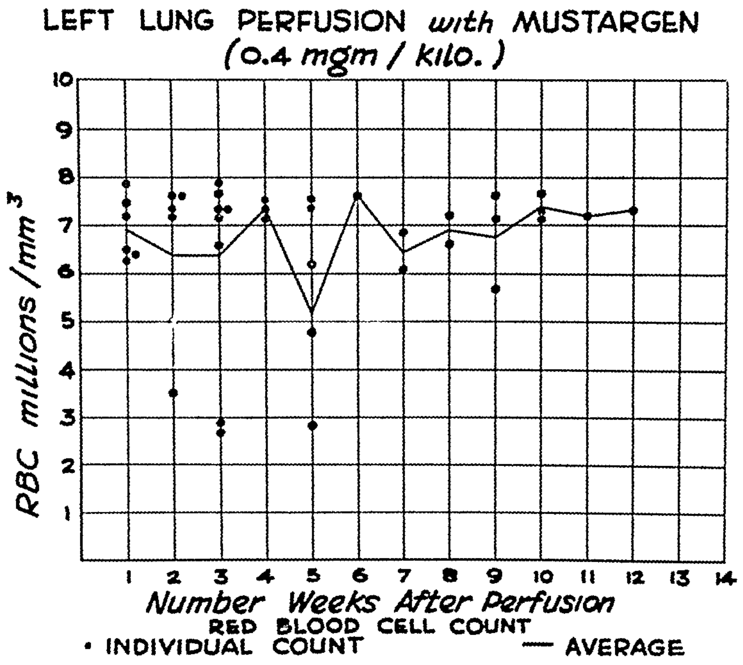
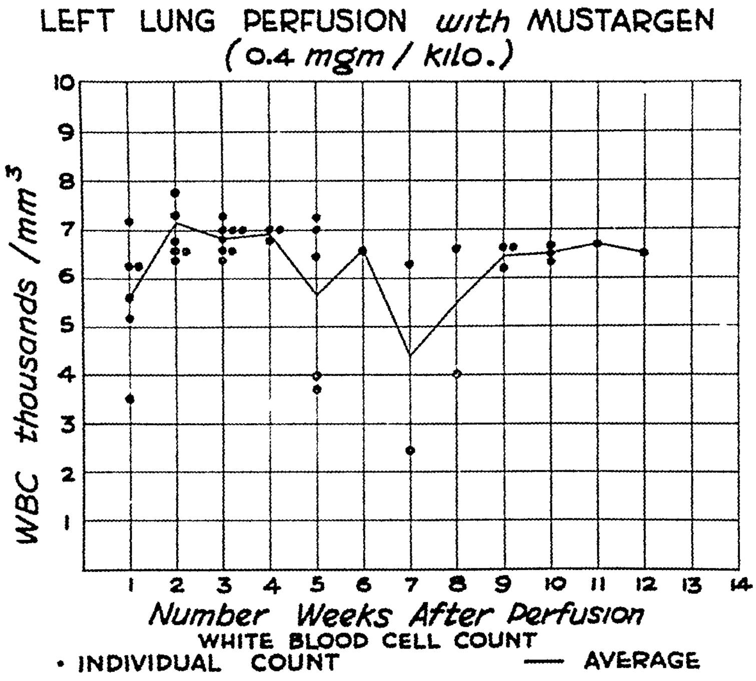

LEFT LUNG PERFUSION with MUSTARGEN
(0.4 mgm / kilo.)
RBC millions / mm³
10
9
8
7
6
5
4
3
2
1
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Number Weeks After Perfusion
RED BLOOD CELL COUNT
• INDIVIDUAL COUNT
— AVERAGE

Fig. 4


LEFT LUNG PERFUSION with MUSTARGEN
(0.4 mgm / kilo.)
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Number Weeks After Perfusion
WHITE BLOOD CELL COUNT
• INDIVIDUAL COUNT
— AVERAGE

Fig. 5.

The relative increase in the maximum tolerated dosage of nitrogen mustard given by isolated perfusion over that given intravenously is based on the relative weight of the left lung compared to the total body weight In dogs, this ratio is 1 to 195

The failure of chrome tagged red blood cells to escape from the perfusion circuit to the general circulation is surprising This tends to support the theory that bronchial veins drain into the pulmonary venous system The escape of noncellular elements of the perfusate via the lymphatics is the subject of a later report

The effects of this type of administration of chemotherapeutic agents on lung tumor await clinical application Palliation is all that can be hoped for using existing compounds However, it is to be expected that a regression and even reduction in size of the lesion may make certain tumors resectable at a later date [3]

The experiments described supply a laboratory preparation for study of the effect of specific agents on lung tissue and furnish a method of deriving basic information for each agent before clinical application

SUMMARY

1 An experimental method for the isolated perfusion of one lung with high concentrations of chemotherapeutic agents for the palliation of cancer is presented

2 Concentrations of nitrogen mustard, two hundred times that tolerated by intravenous injection, were given without the toxic effect of bone marrow depression

3 Radioactive chrome tagged red blood cells do not escape the perfusion circuit in this technique

4 Nitrogen mustard, 0 4 mg per kilogram of total body weight, dissolved in isotonic saline is the maximum tolerated dose in perfusion of the dog's lung

5 The method provides a laboratory bioassay technique for existing chemotherapeutic agents, as well as experimental ones, to be used in palliation of lung cancer

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SEVERE CRUSHING INJURIES OF THE CHEST

A Simple Method of Stabilization

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SEVERE crushing injuries of the chest have become more important to physicians in recent years because of the increasing incidence of major thoracic trauma attendant with high speed vehicular accidents. The high mortality and morbidity associated with such injuries emphasize the necessity for the general practitioner and the general surgeon to be familiar with the management of such injuries. Proctor and London[1] report that of 344,000 injuries treated during the 9-year period 1944-1952, there were only 8 chest injuries with paradoxical respiration requiring surgical treatment. Rives and Kahle,[2] reporting in 1939 on chest injuries following automobile accidents, found that of 16,000 accident patients seen in New Orleans Charity Hospital accident room in a 6-month period, only 24 required hospitalization. On the other hand, Chandler[3] states that chest injuries comprise 25 per cent of all traffic deaths. Chest injuries of the crushing type, such as rib fractures associated with pleural or lung complications, are generally conceded to carry a 10 to 20 per cent mortality rate.[4] As automobiles continue to increase in horsepower, it appears reasonable to conclude that severe crushing injuries of the chest will continue to increase in frequency.

In the 3-year period 1955-1958, there were 154 cases of nonpenetrating chest trauma of sufficient severity to require hospitalization that were admitted to the Louisiana State University Thoracic Surgical service of New Orleans Charity Hospital. It would be impractical to ascertain exactly how many victims of nonpenetrating chest trauma were treated in the accident room without hospitalization, but a conservative estimate would place it at approximately twice the number of those admitted. This estimate is based both on observations by the authors and by the ratio of 3 to 1 found by previous investigators from this institution over a shorter period of time.[2] However, it is readily apparent without resort to statistical analysis that severe thoracic trauma is on the increase.

Of the 154 patients admitted, there were 39 cases involving either a flail chest, or a fractured sternum. There were 8 fractures of the sternum with

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hemothorax, one case of fractured sternum with hemopneumothorax, and one case of fractured sternum with injury to the heart There were 10 cases of flail chest with paradoxical motion but without intrathoracic injury, 2 cases of flail chest with hemothorax, 2 with pneumothorax, 7 with hemopneumothorax, 1 with diaphragmatic rupture, and 2 with cardiac injury Of these 39 patients, 15 required external traction of some sort to stabilize the chest wall, 9 required sandbags for stabilization, and 2 required open thoracotomy The remaining 13 required no type of stabilization, either because of the location of the unstable area or because of minimal degree of paradoxical respiration All patients with hemothorax, pneumothorax, or hemopneumothorax were treated with either single or multiple thoracenteses or with closed intercostal catheter drainage into a water trap, or with appropriate negative pressure suction Of the 39 cases of severe crushing injuries of the chest there was one death Autopsy revealed a severe cerebral laceration in addition to the chest injury

Intelligent management of crushing injuries of the chest requires a thorough knowledge of the normal physiology of respiration and of the disturbances of the physiology brought about by the particular type of injury under consideration[5, 6] The chest wall is "stove in" so that it loses its rigidity and becomes a flail chest If the crushing force is from the lateral direction, the pathology of the injury usually consists of fractures in at least two places of multiple adjacent ribs on the side involved This results in a central portion of the chest wall which is floating This floating section moves in and out with respiration in a reverse or paradoxical direction to the rest of the chest wall This type of respiration markedly decreases the efficiency of ventilation and is usually accompanied by severe pain that renders the coughing mechanism ineffectual More often than not there is associated a hemothorax of considerable degree together with marked contusion and often laceration of the lung, with extravasation of blood, edema, and retention of secretions[6] in the tracheobronchial tree

If the blow is directly over the sternum, as frequently occurs in steering wheel injuries, fractures of the sternum may occur This type of injury is most frequently associated with bilateral costochondral fractures, usually from the first rib down, resulting in an extreme flailing of the anterior portion of the chest wall

Recognizing the above concept of the disturbed physiology resulting from the flail chest with paradoxical motion it becomes evident that large areas of flailing must be stabilized in order to restore as closely as possible the normal physiology The surprising thing to the physician observing this phenomenon for the first time is the amount of respiratory distress, anxiety, pain and shock which can and does result on occasions from apparently small areas of paradoxical chest movement One is equally impressed by the marked improvement in respiration, lessening of anxiety and pain, mental clearing, and the return of normal cardiac action and blood pressure following some form of external fixation of the flailing segment of chest wall.

As can be seen from the treatment employed in our cases, external fixation may be accomplished utilizing a variety of methods. A perusal of the literature reveals many proposed methods of fixation, ranging from simple manual pressure over the flailing area as an emergency method, adhesive strapping of the involved side, sandbags to compress and stabilize the involved weakened segment, rolling the patient onto the flailing area,[7] traction exerted on stainless steel pins passed through the pectoral muscles over the crushed area,[8] towel clips or wires passed around the ribs or sternum in the involved area,[9] cup hooks used for sternal traction,[10] internal fixation of fractured ribs by intramedullary pins and/or wiring of fragments,[11] to application of metal plates to the fragments of fractured sternum.[12]

We have utilized manual pressure as well as turning the patient onto the involved side so as to splint the thoracic wall by the patient's own weight. This is particularly applicable in posterior fractures. Here we have the heavy thoracic muscles which act as a splint to prevent paradoxical motion, or minimize its extent.

We have used sandbags applied over a lateral or anterolateral area of flailing to compress and stabilize the area with good results. It must be admitted that with sandbags the area of compression causes a decreased volume of the involved hemithorax and a consequent decrease in the exchange of air on that side. However, the vicious and dangerous cycle of paradoxical motion, mediastinal flutter, and "pendlehuft" motion is eliminated and more than compensates for the slight decrease in total lung volume on the involved side. Adhesive strapping is mentioned only to condemn it as anything other than an emergency measure for short periods of time in order to transport a patient from the scene of an accident to a hospital. Adhesive strapping, to be effective, must be carried completely around the involved side and past the midline onto the normal side both anteriorly and posteriorly. This compresses and restricts respiratory motion over a large area of normal chest wall as well as over the flailing portion. The use of rib belts, girdles, or other encircling splints is also condemned. Traction exerted on Steinman pins passed through the pectoral muscles is particularly useful in large anterior flailing chest wall segments.[8] We have used this method on occasion in addition to a method of sternal traction which will be described later. This method of traction in anterolateral segments is preferred where sandbagging seems inadequate. Towel clips applied to the ribs or sternum have been used in the past,[9] but they have been used in the present series only as emergency measures until some other method of traction could be instituted. Our chief objection to towel clips and to wires lies in the fact that both clips and wire have a tendency to cut through the tissues, even through bone and cartilage, and have at times come completely loose in as little as 48 hours, which is considered inadequate time for stabilization of a flailing chest. We have had no experience with intramedullary pins or metal plates. Thoracotomy, with its attendant added risk, is reserved for those patients having either actual loss of chest wall requiring surgery for adequate closure of a penetrating wound, or intrathoracic complications which make immediate thoracotomy mandatory. In these cases we have resorted to wiring of the fractured rib fragments with very satisfactory results.[11]

For the last 10 years, we have utilized a simple method of sternal traction which we think offers many advantages, particularly in fractures of the sternum with flailing and in fractures over large segments of the costochondral area. In 1949, two of us (L. S. and M. S.) after observing the use of external fixation of the mandible by the maxillofacial surgeons adapted this principle to external fixation of sternal fractures and extended its use to sternal traction for such fractures and for costochondral fractures.

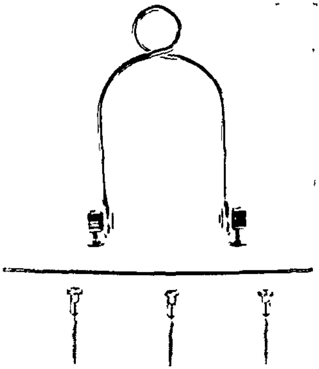

Fig. 1.

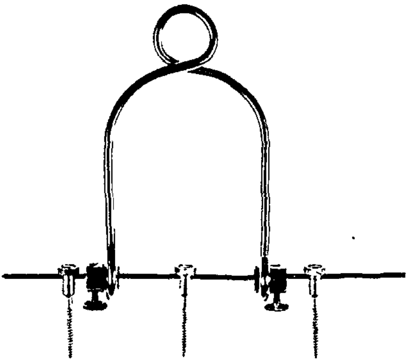

Fig. 2.

Fig 1.—Bigelow screws—metal bar and traction spreader unassembled
Fig. 2 —Bigelow screws—metal bar and traction spreader assembled

The equipment used consists of Bigelow screws,* a pliable aluminum bar which fits into the slotted screws, a traction spreader (Fig. 1), a drill and bit, screwdriver, Balkan frame and weights. Everything except the Bigelow screws and bar are standard hospital equipment. The screws and bars are standard equipment on a maxillofacial service and are relatively inexpensive. On our service, a complete set is always kept sterile in the emergency accident room. Illustrated in Fig. 2, are the Bigelow screws, bar, and spreader. The screws are self-threading and each is provided with a slotted head and a retaining nut which screws over the slotted head.

The technique of insertion of the screws into the sternum is simple, requires only small amounts of local anesthesia, and is relatively bloodless.

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*Bigelow screws manufactured by Austenal Laboratories, Inc., Surgical Division, 224 East 39th Street, New York 16, N. Y.

Utilizing local anesthesia, skin wheals are raised at the proposed sites of insertion of the screws. Usually two screws are inserted in the midline above and two below the site of a sternal fracture. On occasion the fragments may be so comminuted that only one screw may be placed in a fragment. On rare occasions, because of multiple fragments, more than four screws must be used (Fig. 3). Anesthesia is infiltrated down to the periosteum of the sternum at the proposed sites of screw insertion. At each site, a small stab wound is made down to the sternum and a hand drill with the Crutchfield drill point* is used to perforate the anterior cortex of the sternum. The drill point is guarded so effectively that there is minimal danger of penetrating any further than the anterior cortex. The Bigelow screw is then inserted into each hole so formed and screwed into place. When the posterior cortex of the sternum is encountered there is a very definite sensation of increased resistance, and there is a lessening of this resistance when the posterior cortex is penetrated by the screw. Thus, with a modicum of caution and tactile sense, the operator may blindly insert the screw far enough to ensure a firm, strong fit, yet not so far as to impinge upon the heart or great vessels. If desired, a lateral x-ray of the sternum may be utilized to check the depth of the screws. However, we do not find this necessary. After insertion of all screws, the slots in the heads of the screws are aligned. The malleable

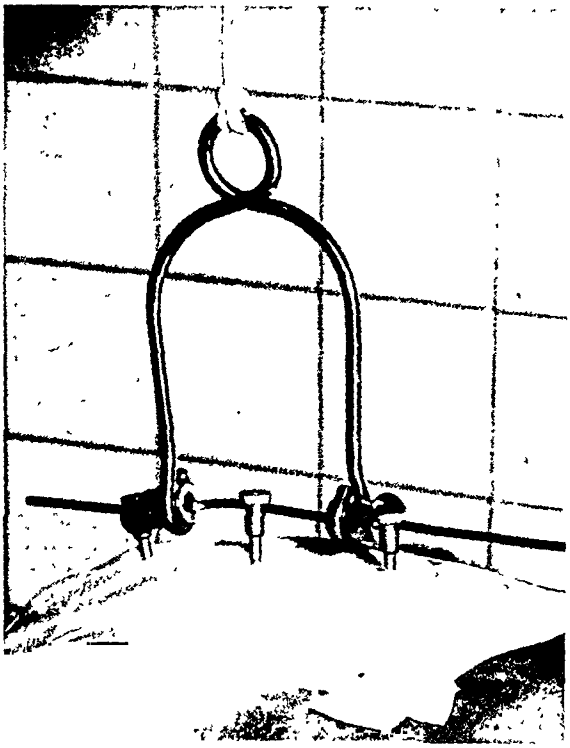

Fig. 3.—Blown up view of traction apparatus applied to sternum.

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*Crutchfield drill point manufactured by Codman and Shurtleff, Inc., 104 Brookline Avenue, Boston 15, Mass.

bar is fitted into the slots, bending the bar as necessary to fit the slots. The retaining nuts are screwed onto the head of the screws so as to retain the bar in place. Not infrequently, in the case of sternal fractures with paradoxical motion, no further fixation is needed. However, should costochondral or parasternal chondral fractures exist, traction will be necessary. This is accomplished by placing the patient in an orthopedic bed and running a rope from a clevis placed on the malleable bar up to an overhead pulley, thence to a pulley at the foot of the bed and adding from three to five pounds of weight as may be needed to stabilize the chest. In the case of parasternal and costochondral fractures, the traction on the sternum is extended through the soft tissues of the anterior chest wall to the site of the fracture. On rare occasions the segment of flailing has been so large that lateral muscle traction of the Hudson type[5] has also been necessary. A double bar with Bigelow screws may be necessary on rare occasion (Figs. 4 and 5).

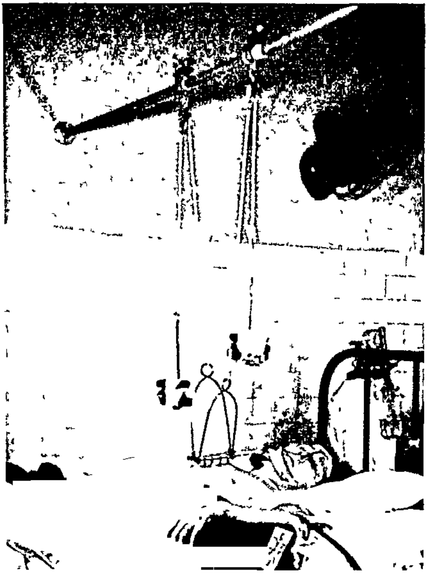

Fig 4—Double bar traction to sternum with bilateral costochondral rib fractures and with weights attached

We feel that the advantage of simplicity of performance of this procedure and the avoidance of a general anesthesia should definitely be considered as opposed to thoracotomy with internal fixation. We consider that the advantages of this procedure, as opposed to wires or towel clips, lie not only in simplicity and avoidance of possible pneumothorax, but primarily in the fact that properly placed Bigelow screws will remain in place much longer without cutting through the tissues. We have frequently utilized up to 12 pounds of traction for 2 weeks. This period allows sufficient healing to occur so that paradoxical motion is eliminated when the traction is released. Subsequently the screws and external fixation bar may be left in place for another 2 weeks to ensure firm union of a sternal fracture. Occasionally there may be a semipurulent drainage from the screw holes for a few days, but we have had no cases of osteomyelitis We believe that the extra fixation afforded by the malleable bar fitting into the screw heads provides a definite advantage over the modified cup hooks described by Rook[10] and utilized by Proctor and London.[1]

In addition to the use of some form of fixation of the chest wall, attention must be centered on the maintenance of an adequate airway. This has been emphasized by others.[13, 14] We frequently utilize nasotracheal suction and/or bronchoscopy It has been our experience that the vast majority of these patients cannot be kept free of accumulated secretions without repeated nasotracheal aspiration. In addition to predisposing to laryngeal edema and further respiratory embarrassment, nasotracheal aspiration requires the constant attendance of a skilled and energetic nurse or physician. The same, with even more emphasis on the skill and energy of the physician, is true of repeated bronchoscopy. Still another shortcoming of these modes of treatment lies in the fact that they do nothing to cut down on the dead air space. The addition of a tracheotomy has been shown to decrease the dead air space by 75 to 150 c.c.[13] Aspiration of secretions may then be carried out by relatively unskilled help, there is less resistance to air movement, hence less

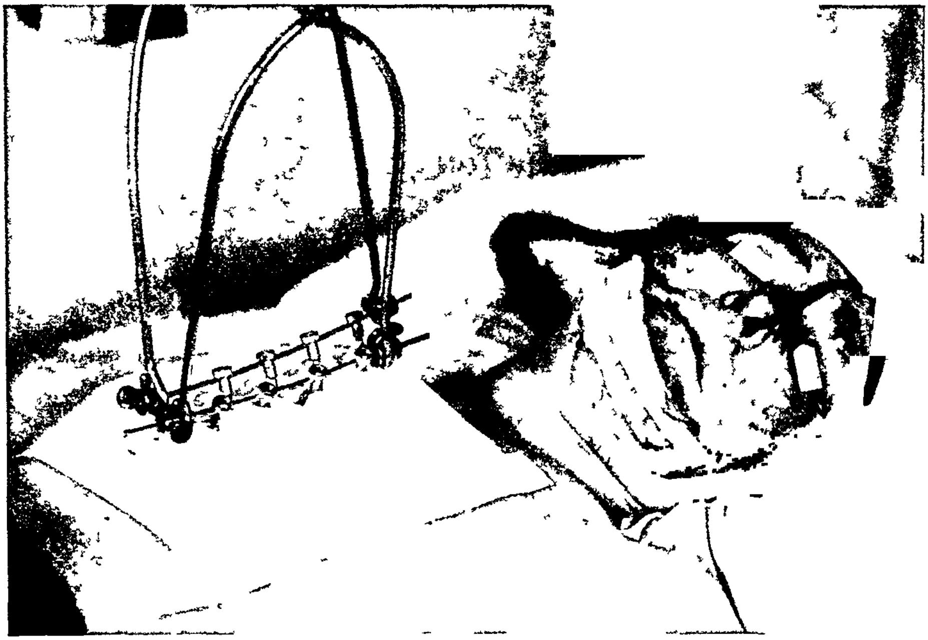

Fig 5—Blown up view of double bar traction to sternum in bilateral costochondral fracture with severe flailing of chest

paradox, and oxygen consumption is decreased because of decreased muscular exertion needed to breathe.[14] Therefore, if the patient is having significant flailing or any signs of respiratory distress or hypoxia, we routinely resort to early tracheotomy.

The treatment of shock should follow the usual lines of blood replacement, nasal or tracheal oxygen, relief of pain, etc. Frequently, the treatment of the primary injury of a flail chest will alleviate the clinical signs of shock without blood or plasma expanders having to be used.

The treatment of intrathoracic complications, such as hemothorax and/or pneumothorax, must, of course, be handled intelligently in these cases. If significant hemothorax or tension pneumothorax exists, we prefer to utilize intercostal catheter and water trap drainage with appropriate suction.[2] However, in cases of hemothorax and/or pneumothorax of lesser degree we often use either single or multiple thoracenteses followed by frequent, portable x-ray studies. The details of treatment of complications are not the province of this paper. Suffice it to say that we believe the best method of sealing off a leak of air or blood from the lung lies in rapid re-expansion of the lung, approximating visceral to parietal pleura. Whether this is accomplished by needle aspiration or intercostal drainage is relatively unimportant. Thus we individualize the treatment of these complications.

Necessarily, an injury of sufficient severity to crush a chest will usually produce multiple injuries. The appropriate treatment of orthopedic, abdominal, neurological, genitourinary, and maxillofacial injuries must be carried out concomitantly. We would agree with Daughtry[6] that joint cooperation and consultation between various specialists should be utilized. However, in general, the most rapid killer in the group of multiple injuries will usually be the chest injury unless it is handled intelligently and promptly. The general surgeon with a good orientation toward thoracic physiology, or in consultation with the thoracic surgeon, should be able to treat adequately these severe and dangerous injuries.

SUMMARY

Severe crushing injuries of the thorax are definitely on the increase. As a result, flail chest with paradoxical motion is seen more often.

Disturbances in respiratory physiology occur and it is mandatory that these be remedied immediately. In order to do this, the area of flailing must be stabilized.

Although many methods of stabilization have been reported, and are currently used, none are completely satisfactory.

A simple method of sternal fixation and traction utilizing the Bigelow screws and bar is presented, and our experiences with this method are related.

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MIDDLE LOBECTOMY FOR TUBERCULOSIS IN CHILDHOOD

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REVIEW OF THE LITERATURE

THE middle lobe syndrome has received a great deal of attention since Hampton and King[1] described the roentgenographic changes consistent with atelectasis of the middle lobe and demonstrated that what was called interlobar empyema, pleural fluid, or thickened interlobar septa was generally an airless middle lobe. Kent,[2] in 1942, discussed 10 cases of atelectasis of various lobes associated with tuberculous enlarged hilar nodes in childhood. He showed that the homogeneous density seen in x-ray studies did not represent tuberculous pneumonia. Seven of his 10 patients became bronchiectatic in the area of involvement after 7 months or more of chronic bronchial occlusion. He felt that the prognosis was favorable without operation. Jones, Peck, and Willis[3] also demonstrated bronchiectasis, or no filling on bronchogram, in 70 per cent of a sizable series of cases of primary tuberculosis with intrinsic or extrinsic bronchial obstruction examined 1 year after the original diagnosis.

The pathogenesis of endobronchial tuberculosis in children is presented in a very thorough and complete article by Daly, Brown, Lincoln, and Wilking.[4] They prove bronchoscopically that endobronchial tuberculosis is common in children with tuberculosis, particularly in younger children, and that the middle lobe is most frequently involved. Bronchoscopy revealed compression or fixation by nodes, sometimes obstruction by mucosal inflammation, granuloma, caseous material extruded from a ruptured node, or a fibrous stricture. Progression from one lesion to another was observed. Late manifestations of bronchiectasis, persistent roentgenographic shadows, productive cough, râles, and recurrent lung infection are described.

Graham, Burford, and Mayer,[5] in 1948, reported 12 resections for the middle lobe syndrome, all in adults, all with good results, and none for tuberculosis. They emphasized the vicious circle of obstruction causing infection which resulted in more lymphadenitis. Shaw and Paulson,[6] in 1949, stated that a collapsed middle lobe may or may not be associated with enlarged or calcified lymph nodes, may be due to mucosal inflammation, foreign body, or any other form of obstruction. Middle lobectomy was recommended and chronic pneumonitis, atelectasis, fibrosis, and bronchiectasis were described in the resected

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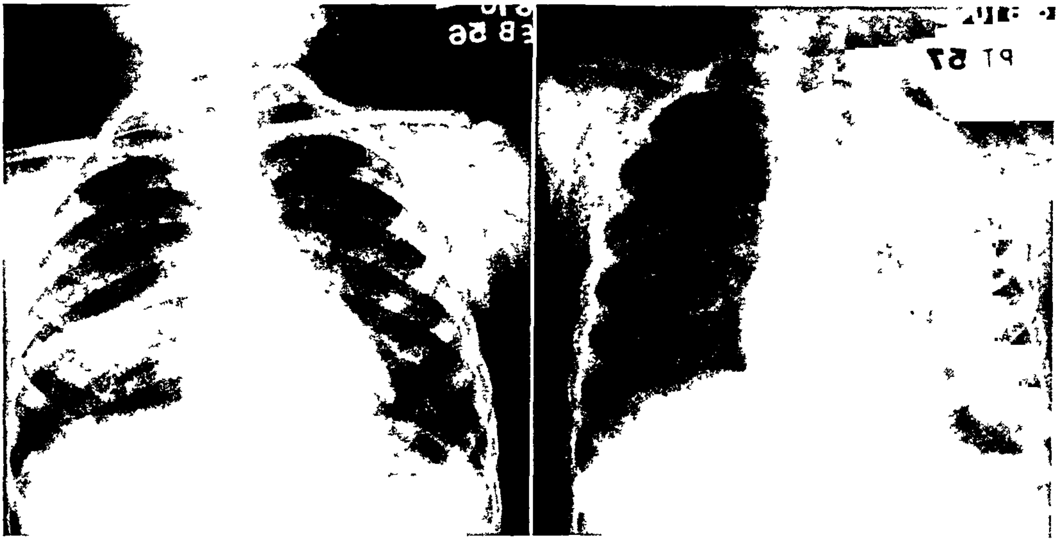
specimens. Resection is also advised for the middle lobe syndrome by Harper, Condon, and Wierman,[7] who feel there is no definite syndrome associated with middle lobe collapse. Tuberculosis was found in 3 of 26 specimens, the remaining ones showing chronic pulmonary suppuration and bronchiectasis with fibrosis.

There is no unanimity of opinion concerning the treatment of choice in middle lobe atelectasis due to childhood tuberculosis. Perusal of the case reports will show that our 3 patients were discussed at great length repeatedly before undergoing thoracotomy and, in each case, surgery was performed although several physicians did not concur. In view of the controversy these little patients stimulated, an examination of their cases seems worth while.



A *B.*

Fig 1.—Case 2 *A*, Before surgery *B*, One year after surgery.

CASE REPORTS

CASE 1.—This 4 year old patient contracted tuberculosis in Germany at the age of 15 months. He received streptomycin and para-aminosalicylic acid (SM-PAS) therapy for 14 months. Two years later, due to roentgenographic changes and a palpable lymph node in his neck, he was admitted to Fitzsimons Army Hospital. At this time the middle lobe was atelectatic. The child was asymptomatic.

Physical examination revealed an occasional wheeze in the right middle lobe area, bacteriologic examinations were negative, bronchograms demonstrated no filling of the middle lobe, and bronchoscopy showed granulation tissue obstructing the right middle lobe bronchus. Repeat bronchoscopy 5 months later showed a clean, narrowed right middle lobe orifice.

The patient was presented at staff conference four times in 5 months, and there was wide disagreement regarding the need for surgical intervention. A middle lobectomy was performed, since this was the desire of the majority. A nodose lesion was also locally excised from the anterior basal segment. The postoperative course was benign. At surgery, the middle lobe orifice was noted to be markedly stenotic.

Pathologic examination revealed bronchiectasis, grossly, and pulmonary fibrosis, microscopically, in the middle lobe. Tubercle bacilli were identified in the lesion from the anterior basal segment.

X-ray studies 3 years later revealed only minimal pleural changes at the right base. The child is well.

Case 2.—This 3-year-old child contracted tuberculosis in Turkey when but a few months old. She arrived at Valley Forge Army Hospital 2 years later on SM-PAS therapy. She was asymptomatic. Films dated February, 1956, showed a right middle and lower lobe pneumonic infiltrate. The lower lobe lesion cleared but middle lobe opacity was still present 7 months later. Bronchograms did not reveal bronchiectasis. Gastric cultures were positive for tubercle bacilli. Bronchoscopy failed to reveal the etiology of the middle lobe atelectasis.

Lobectomy was recommended the first time this patient was presented at staff conference. *Thoracotomy 8 months after admission revealed a collapsed lateral segment of* the middle lobe. In the resected specimen, a fibrin plug was found occluding the bronchus. There was no evidence of extrinsic pressure or intraluminal disease. Microscopically, no evidence of tuberculosis was found in the resected specimen. The postoperative course was uncomplicated, and 1-year follow-up revealed a normal child with a normal roentgenogram of the chest.

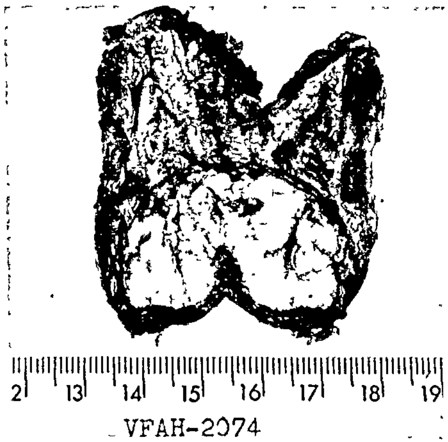


Fig 2—Case 3 Middle lobe opened to show caseo-cavitary lesion.

Case 3.—This 2-year-old Japanese-American child who was born in Japan had a chest roentgenogram taken prior to circumcision. This revealed what was interpreted as a pneumonic process in the middle lobe. As PPD 1 was found to be positive, he was transferred to Valley Forge Army Hospital where one gastric culture revealed *Mycobacterium tuberculosis* resistant to isonicotinic acid hydrazide (INH) as well as being catalase negative. The child was asymptomatic. INH-PAS therapy for 6 months did not alter the roentgenographic appearance of middle lobe atelectasis.

At staff conference this child was considered repeatedly for surgery at the request of the Pediatric Service. A variety of opinions were expressed by house and consultant staff and, although lobectomy was finally authorized, no unanimity of opinion was reached. A middle lobectomy was performed after 7 months of antituberculous therapy. A large caseo-cavitary lesion with wide open bronchial communication was found. The postoperative course was benign and roentgenograms made 1 month after surgery revealed only minimal postoperative pleural changes.

DISCUSSION

It is apparent that atelectasis of the middle lobe may be an asymptomatic lesion. A proper etiologic diagnosis is not always possible prior to surgery. Had we known that a fibrin plug caused the atelectasis in Case 2, surgery would not have been performed. On the other hand, all would have recommended surgery in Case 3 had we known that there was an open cavitary lesion in the middle lobe. On the basis of probability, one would expect to find such lesions as bronchiectasis, pulmonary fibrosis, bronchostenosis, or extrinsic lymph node pressure, as reported by others.

It is well known that patients of all ages do well after middle lobectomy, since the architectural arrangement almost precludes the commonest postoperative complications, bronchopleural fistula and space problems. These young children had smooth postoperative courses, can proceed through life without demonstrable tuberculous lesions, and further tuberculous activity may have been avoided in 2 cases.

As a warning, this type of surgery is often not easy. Dense fibrosis about the hilum makes the identification and isolation of arterial branches and the middle lobe bronchus a tedious and time-consuming process.

SUMMARY

Three cases of middle lobe syndrome from primary tuberculosis in infancy and young childhood are presented. The treatment of choice is lobectomy after an adequate period of antituberculous therapy. The etiology of the atelectasis is multiple. The pathologic findings vary and are not always predictable. An uneventful postoperative course can be anticipated.

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PARTIAL RESECTION OF THE ONLY REMAINING LUNG WITH THE AID OF RESPIRATOR TREATMENT

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INDICATIONS

RESPIRATOR treatment is indicated in every case of ventilatory insufficiency regardless of its cause, if bronchial aspirations and a tracheostomy alone do not bring the pCO_2 back to a normal level

Ventilatory insufficiency will occasionally be found in the postoperative course after any extensive intrathoracic procedure on either the lung and the chest wall the heart, the great vessels, or the esophagus At this stage, when the patient's own respiratory work is insufficient and accompanied by carbon dioxide retention respirator treatment may be lifesaving

When is then the right moment for introduction of artificial ventilation? Clinical experience and a careful observation of these patients will usually make the decision easy If one is doubtful, an arterial puncture with determination of the pCO_2 is helpful

Sufficient experience has now accumulated so as to make possible, in certain cases the decision of postoperative respirator treatment even before the operation In this event, all respiratory work is taken away from the patient in the postoperative period and an adequate ventilation is guaranteed Furthermore the patient is relieved of all effort needed to bring up accumulated secretion as this will be aspirated at intervals There will be no pain as the patient can receive sufficient morphia to control it without regard to its effect on the respiratory center Resection of part of the only remaining lung is considered a clear indication for postoperative respirator treatment The first such patient operated upon before the introduction of the respirator in thoracic surgery died on the second day due to an aspiration pneumonia Four subsequent patients have survived, mainly due to the respirator treatment

TECHNIQUE

After an experience of more than 200 cases of postoperative respirator treatment, certain technical details have proved important

The Tracheostomy —

A transverse skin incision is preferred It should be placed as low down on the neck as possible for cosmetic reasons In some cases, the skin will be

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fixed to the trachea when the cannula is removed causing discomfort to the patient when swallowing. Then a plastic operation is required to free the skin from the trachea, and to interpose muscles in the midline between the skin and the trachea. This plastic re-operation cannot be satisfactorily performed if a vertical incision has been used. Furthermore, keloid formation is more common after a vertical incision.

In the beginning, only an incision was made in the trachea; but one patient with pulmonary complications after the closure of an atrial septal defect with the aid of a heart-lung machine was suffocated when the cannula slipped out and the inflated cuff compressed the trachea. Therefore, we always make a hole in trachea but, instead of excising a portion of the anterior wall of the trachea, this portion is left attached to the trachea inferiorly, constituting a flap of the tracheal wall fixed to the skin by a catgut suture (Fig. 1).

Advantages are (1) preventing the cannula from slipping down in front of the trachea below the tracheostomy; (2) the patient can breathe more easily through the opening in the trachea even in the first days if the cannula should become dislocated; and (3) if the flap is 4 to 5 mm. broad and has its base inferiorly, an open tracheostomy facilitates the exchange of the cannula. This flap has not caused excessive granulation tissue and stricture formation. On the contrary, if the cannula is not left in place too long the flap will fall back and prevent excessive formation of granulation tissue through the stoma.

It is very important to make the hole in the trachea as high as possible, preferably through the second, third, and fourth cartilages (Fig. 1, *B*). In cases in which a low tracheostomy has been performed, it has been very difficult to keep the cannula in place and the connection airtight. The rubber cuff on the silver cannula may be partly outside the trachea if the tracheostomy is too low. When the cuff is inflated, the cannula may be pushed out of the trachea (Fig. 1, *C*). In one case in which the tracheostomy was too low, the cannula was repeatedly displaced when the cuff was inflated and the wound had to be packed with gauze around the cannula to make the connection somewhat airtight.

A firm fixation of the cannula by the band around the neck is especially important in children difficult to keep in the same position. This band can quickly be cut and the cannula removed if occluded.

The Cannula.—

Rubber tubes should not be used due to the following disadvantages: (a) they are often too long, causing occlusion of one (the left) main bronchus; (b) they may not have the right curvature, causing pressure on the posterior membranous wall of the trachea with an esophago-tracheal fistula as a result; and (c) a rubber tube will soon be narrowed by dried up secretion.

A silver cannula, on the other hand, is easily kept open, as the inner cannula can be taken out daily for cleaning. We have never seen an esophago-tracheal fistula caused by a rubber-cuffed silver cannula. The silver

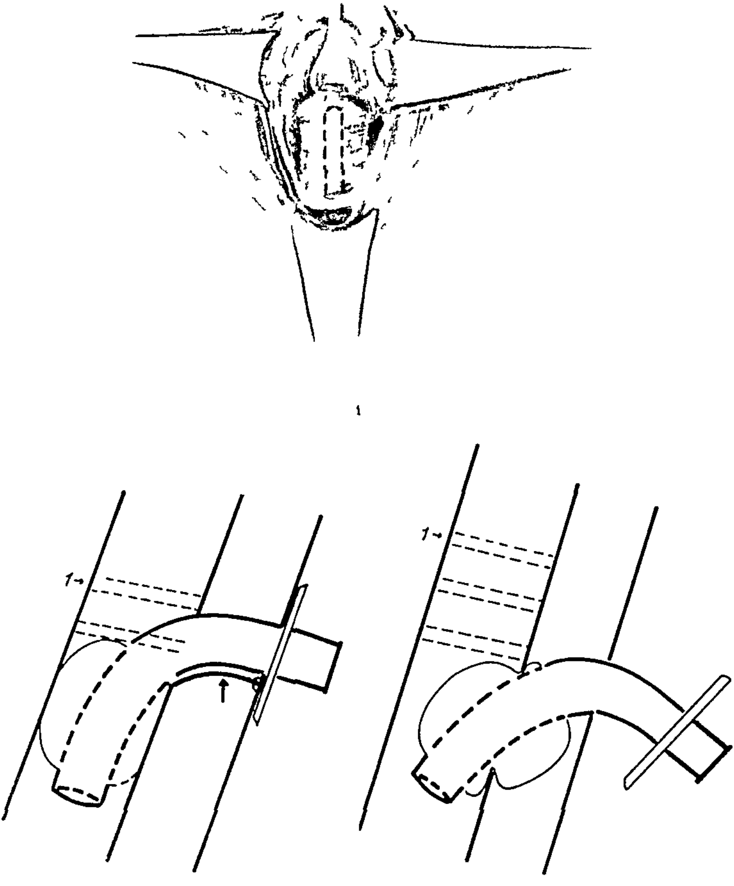

Fig 1A —Diagram of the incision in the trachea through the second and third cartilages with a flap of the anterior tracheal wall which may be sutured to the skin

B Diagram of the correct position of the cannula in the trachea Observe the anterior tracheal flap (→) which will prevent the cannula being dislocated to the space in front of trachea the flap will keep the stoma open and facilitate exchange of the cannula. With the high incision including the second down to the fourth tracheal rings the rubber cuff will stay inside the trachea

C, Diagram of the wrong position with a low tracheostomy and the rubber cuff partly outside the tracheal lumen thus displacing the cannula outward when the cuff is inflated fixed to the trachea when the cannula is removed causing discomfort to the patient when swallowing. Then a plastic operation is required to free the skin from the trachea, and to interpose muscles in the midline between the skin and the trachea. This plastic re-operation cannot be satisfactorily performed if a vertical incision has been used. Furthermore, keloid formation is more common after a vertical incision.

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Advantages are (1) preventing the cannula from slipping down in front of the trachea below the tracheostomy; (2) the patient can breathe more easily through the opening in the trachea even in the first days if the cannula should become dislocated; and (3) if the flap is 4 to 5 mm. broad and has its base inferiorly, an open tracheostomy facilitates the exchange of the cannula. This flap has not caused excessive granulation tissue and stricture formation. On the contrary, if the cannula is not left in place too long the flap will fall back and prevent excessive formation of granulation tissue through the stoma.

It is very important to make the hole in the trachea as high as possible, preferably through the second, third, and fourth cartilages (Fig. 1, *B*). In cases in which a low tracheostomy has been performed, it has been very difficult to keep the cannula in place and the connection airtight. The rubber cuff on the silver cannula may be partly outside the trachea if the tracheostomy is too low. When the cuff is inflated, the cannula may be pushed out of the trachea (Fig. 1, *C*). In one case in which the tracheostomy was too low, the cannula was repeatedly displaced when the cuff was inflated and the wound had to be packed with gauze around the cannula to make the connection somewhat airtight.

A firm fixation of the cannula by the band around the neck is especially important in children difficult to keep in the same position. This band can quickly be cut and the cannula removed if occluded.

The Cannula.—

Rubber tubes should not be used due to the following disadvantages: (a) they are often too long, causing occlusion of one (the left) main bronchus; (b) they may not have the right curvature, causing pressure on the posterior membranous wall of the trachea with an esophago-tracheal fistula as a result; and (c) a rubber tube will soon be narrowed by dried up secretion.

A silver cannula, on the other hand, is easily kept open, as the inner cannula can be taken out daily for cleaning. We have never seen an esophago-tracheal fistula caused by a rubber-cuffed silver cannula. The silver

1. First, the inspiration must start from a pressure of zero and slowly build up the pressure. In other words, there must not be a sudden pressure explosion with danger of damage to the lung parenchyma. Then a terrific speed of the gas, 7.5 L. per second, is needed to move the normal tidal air in an elastic way without danger for the alveoli. The maximum flow is reached at the maximum pressure.

2. After the maximum pressure and flow comes a period of constant high pressure. "The plateau formation" equalizes the pressure in all areas of the lung and produces an even alveolar ventilation, even in the pressure of partial bronchial obstruction.

3. The expiration may be only passive, or a negative phase is most often added. At the end of expiration the air does not move and the pressure is zero. All credit goes to Engström for having constructed such a respirator, which is the only respirator so far I have seen or tested that fulfills all these criteria (Fig. 3).

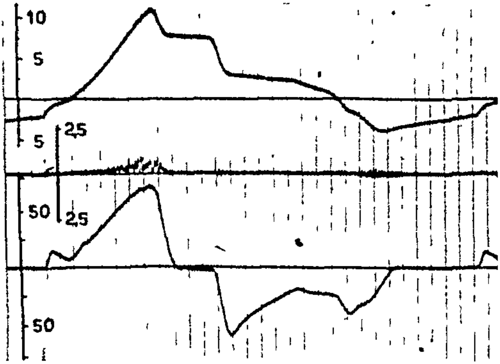

Fig 3.—The *upper* curve shows the intratracheal pressure, the *lower* curve represents the flow utilizing an Engstrom respirator with negative phase during expiration

METHOD

A. *Constant Ventilation.*—

If possible, the patient should be instructed about the details of the respirator treatment before it is instituted. The patient may then better follow the machine. There is usually no difficulty in continuing the respirator treatment directly after an operation. If, however, this treatment is instituted some days after the operation, it may sometimes be difficult to get the patient synchronized with the machine. When the patient works against the respirator either it should be disconnected or the valves should be closed, preventing the patient from inspiring air from outside the machine. Giving repeated doses of morphia every 4 hours relieves all pain as well as making it easy for the patient to synchronize with the machine which will take over all the respiratory work. The frequency and minute volume must be adjusted to the size of the patient. An adult patient usually needs 10 L. ventilation per minute. A mixture of 50 per cent air and 50 per cent oxygen has proved to be satisfactory in most cases.

B. *Airtight Connection.*—

From time to time it is necessary to see that the ventilation is kept constant. The expired volume is measured, and if it is equal to the inspired amount, no leakage in the system is indicated. If the expired volume is less than the inspired volume, there is usually a leak around the rubber cuff on the silver cannula. At every inspiration some gurgling sound may be heard as the gas passes the larynx and out through the mouth or nose instead of into the lung. Careful observation of and listening to the patient may disclose either that the rubber cuff is inflated too little or has ruptured and needs to be exchanged. Obviously the continous delivery of gas must be guaranteed.

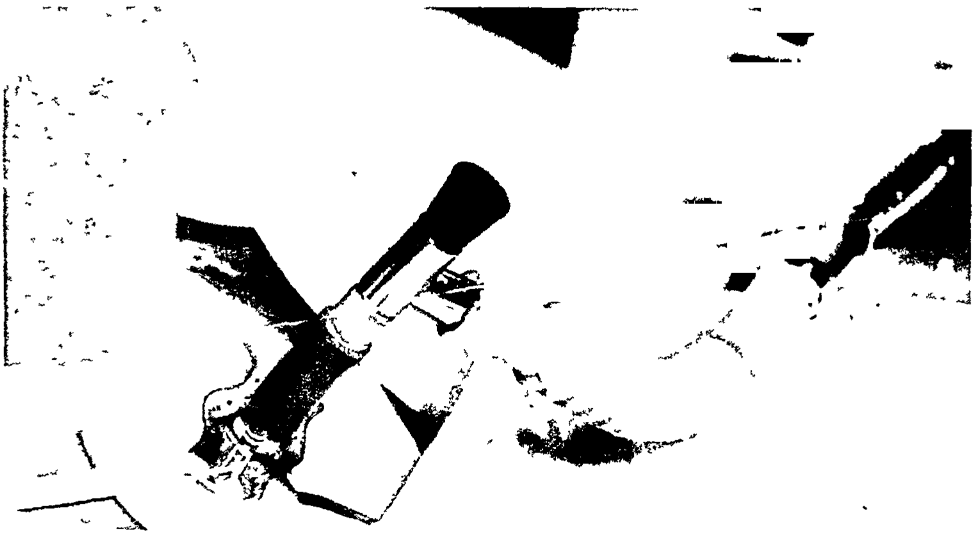

Fig. 4.—Photograph of the connection between the tracheal cannula and the respirator. The cork is removed for introduction of a catheter for aspiration.

C. *Continuous Gas Supply.*—

There have been two accidents, one with a lethal outcome, in which the oxygen supply was emptied while the patient was connected in an airtight manner to the respirator. Half the volume of air needed was not sufficient for a seriously ill patient during the time before detection of the error.

D. *Open Airway.*—

The trachea and the bronchi must be aspirated at intervals. The cannula is therefore connected to the respirator with a T-tube (Fig. 4). One need only remove a cork to introduce a catheter for aspiration. Secretions may

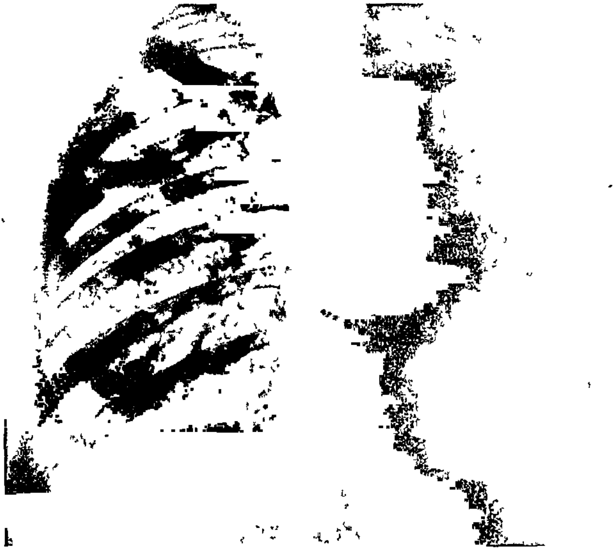

Fig 5A—Case 1 X-ray study of a 26-year-old woman having a giant cavity in the right upper lobe after a left pneumonectomy Organisms were resistant to INH PAS, and streptomycin Cavity represents a completely destroyed right upper lobe

Fig. 5B—Case 1 X-ray study made 1½ years after the operation

dry, causing obstructions in the airway. The inner cannula should be removed for cleaning and boiling daily. The easy passage of the suction catheter shows that the cannula is in the right position and that it is not blocked. From time to time we have removed fibrin clots which filled the cannula. If the cannula is blocked by a clot that cannot be aspirated, the cannula must be removed quickly at which time the clot is usually dislodged with a cough of great force. If not, a bronchoscope is inserted for the removal of the obstruction. If dried up secretions are found, it is most important to inject 10 ml. of saline solution into the trachea. This should then be repeated at intervals.

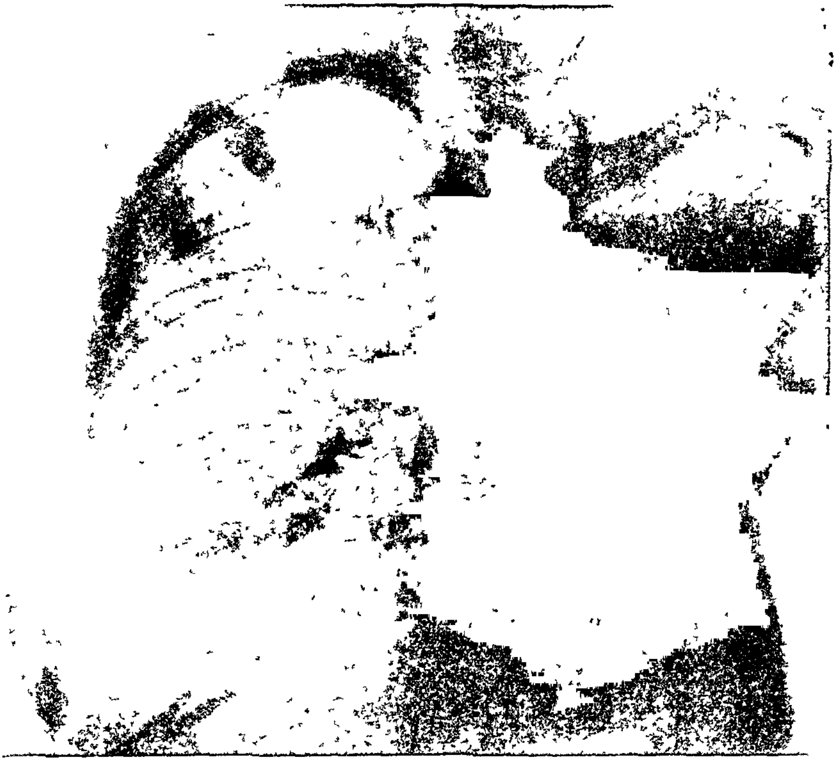

Fig. 6—Case 2. X-ray study of a 29-year-old woman 3 years after left pneumonectomy and right upper lobectomy.

CASE REPORTS

The following cases with partial resection of the only remaining lung represent an indication for institution of respirator treatment immediately after surgery.

Case 1.—A 26-year-old woman with bilateral pulmonary tuberculosis underwent left pneumonectomy in 1956. In 1957, a large cavity appeared in the right upper lobe (Fig. 5A). Organisms were resistant to isonicotinic acid hydrazide, para-aminosalicylic acid, and streptomycin (she had received more than 200 Gm. of streptomycin). A right upper lobectomy was performed in the face-down position, followed by 4 weeks of respirator treatment. The patient was then able to take over the ventilation herself and made

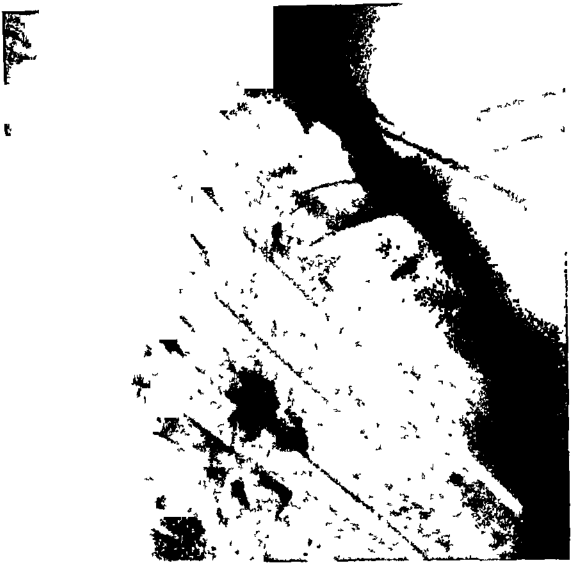

Fig 7A—Case 3 X-ray study demonstrating an apical cavity in the only remaining left lung

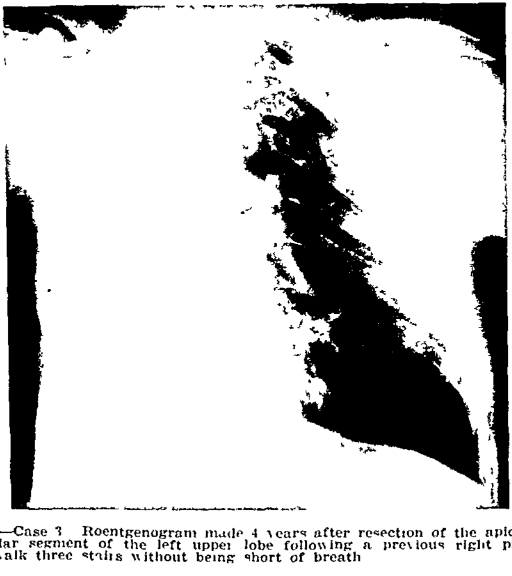

Fig 7B—Case 3 Roentgenogram made 4 years after resection of the apicoposterior and inferior lingular segment of the left upper lobe following a previous right pneumonectomy Patient can walk three stairs without being short of breath

an uneventful recovery. Two years after the operation (Fig. 5*B*) this patient's sputum was negative for tubercle bacilli. She had a normal sedimentation rate (7 mm.), and the vital capacity was 2,200 ml. She had no cough; she was no more dyspneic than before the operation but she felt very short of breath walking upstairs after having had a heavy meal. She worked all day with a 2-hour rest in the middle of the day. She cared for her home and two children, and did the cleaning and washing herself.

CASE 2.—A 29-year-old woman with bilateral pulmonary tuberculosis underwent left upper lobectomy in 1954 and right upper lobectomy in 1955. In 1956 she underwent a reresection of the left side resulting in a total pneumonectomy with an osteoplastic thoracoplasty, as the organisms were streptomycin resistant and she had a residual cavity. Postoperative respirator treatment was needed for 3 weeks. One year later she had a child by cesarean section and 3 years after the last operation she was doing housework, taking care of her child and husband. An x-ray study (Fig. 6) shows the well-functioning remaining two lobes of the right side. The maximal breathing capacity was 65 L. per minute and her sputum was negative. The sedimentation rate was 7 mm.

CASE 3.—A 29-year-old man underwent a righ pneumonectomy in 1954 for pulmonary tuberculosis. In 1955, a tuberculous cavity appeared in the apex of the left lung (Fig. 7*A*). He then underwent a resection of the apicoposterior segment and the inferior lingula segment of the left upper lobe. Postoperative respirator treatment was necessary for 12 days. The patient then made an uneventful recovery and 4 years after the operation he is working full time as a driver, and doing extra work in the evening, mounting television antennas on the roofs of houses. An x-ray study (Fig. 7*B*) shows no active tuberculosis. There is negative sputum, a normal sedimentation rate (2 mm.), and a maximal breathing capacity of 70 L. per minute with a vital capacity of 2,300.

SUMMARY

Partial resection of the only remaining lung for open tuberculous cavities can be performed with safety for the patient as long as tracheostomy with respirator treatment is given in the postoperative period. Patients lose some pulmonary function, but subjectively they do not notice this loss, as the sputum disappears at the same time. All 3 patients have gone back to an active life; one also having delivered a baby, the second able to look after her home and two children, and the third is doing full-time work. All sputa are negative for tubercle bacilli.

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STUDIES OF PULMONARY FUNCTION BEFORE AND AFTER PULMONARY RESECTION IN 450 TUBERCULOUS PATIENTS

II. Case Analysis of Patients With Large Loss of Vital Capacity and Maximum Breathing Capacity

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A PREVIOUS communication[1] described the average loss of pulmonary function resulting from a variety of operations for removal of tuberculous lesions of the lungs. A close correlation was shown between the amount of functioning lung tissue removed and the loss of function, as measured 6 months postoperatively. There is generally little significant decrease of function in segmental and lobectomy operations. More extensive removal of lung tissue, such as bilateral resections and pneumonectomy, may cause rather large loss of function. In any series of resections, a number of complications may occur which are capable of profoundly altering pulmonary function. It is important for the physician referring patients for resection, as well as for the consulting surgeon, to know approximately how much function may be lost in the event of complications arising as a result of resection. It is the purpose of this paper to review the 450 tuberculous patients previously reported and to select for analysis those who had the greatest postoperative loss of vital capacity and maximum breathing capacity.

MATERIAL AND METHODS

The vital statistics and description of the methods used in testing the pulmonary function of the 450 tuberculous patients may be found in the first paper of this series. All patients received pulmonary function screening tests 1 to 2 weeks before resection and at an average time of 6 months after operation. It was shown that within this period most patients regain their maximum function. The patients who suffered the greatest loss of vital capacity and maximum breathing capacity were tabulated. The percentage loss of vital capacity and maximum breathing capacity were added together and will be designated as the combined loss. A cut off level for large combined losses was then selected which included a representative sample for patients receiving each type of operation, excluding pneumonectomy and decortication

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RESULTS

One hundred and eighty-nine patients underwent unilateral segmental operations. Within this group were 9 patients who had an average loss of 18 per cent in vital capacity and 33 per cent in maximum breathing capacity, the maximum combined loss by a single patient in this group was 59 per cent. Lobectomy was performed in 123 patients, 7 had an average loss of 23 per cent in vital capacity and 36 per cent in maximum breathing capacity. The greatest combined loss in this group was 75 per cent. Fifty-three patients were subjected to bilateral segmental resections, 4 had an average loss of 35 per cent in vital capacity and 35 per cent in maximum breathing capacity. The greatest decrease in function in this group was found in 2 patients, each having 75 per cent combined loss. Review of patients undergoing bilateral lobectomy and segmental resection showed that there were 27 in this group, 7 had an average loss of 24 per cent in vital capacity and 33 per cent in maximum breathing capacity, the greatest combined loss was 62 per cent. Those having bilateral lobectomy only numbered 7 and there were 2 with average loss of 49 per cent in vital capacity and 49 per cent in maximum breathing capacity. In most of the patients there was a greater loss of maximum breathing capacity than of vital capacity.

TABLE I. COMPLICATIONS OF VARIOUS TYPES OF PULMONARY RESECTIONS RESULTING IN LARGE LOSS OF VITAL CAPACITY AND MAXIMUM BREATHING CAPACITY

	TOTAL NUMBER	NUMBER WITH LARGE LOSS	AVERAGE LOSS IN VC (%)	AVERAGE LOSS IN MBC (%)	SURGICAL COMPLICATIONS							NO COMPLICATION
					BLEEDING	AIR SPACE	AIR SPACE THORACOPLASTY	ATELECTASIS	ATELECTASIS AND THORACOPLASTY	ADHESIONS OF DIAPHRAGM	DIAPHRAGM PARALYZED	
Segments	189	9	18	33		2	3	1	1			2
Lobectomies	123	7	23	36	1*	1	1			1	1	2
Bilateral segments	53	4	35	35	1*		1			1	1	
Bilateral lobe + seg.	27	7	24	33			1*		1	1	2	2
Bilateral lobes	7†	2	49	49			1					1
Total	399	29			2	3	7	1	.2	3	4	7

*Thorax reopened.

†43 pneumonectomies and 8 decortications not tabulated.

Table I shows the types of surgical complications which seemed primarily responsible for large loss of function in 29 of the 450 tuberculous patients. It is seen that there is a random scatter of complications among the various types of operations. No particular resectional operation can, therefore, be said to favor a specific complication. Intrathoracic bleeding occurred 13 times, requiring reopening of the chest to evacuate the clots and to ensure hemostasis. Extensive adhesions which resulted seem to be responsible for the loss of function in 3 of these patients.

Persistent air space may be defined as the roentgenologic appearance of loculated air usually at the apex, occasionally at the base, which persists for more than a month postoperatively. It is postulated that a tiny air leak is responsible for such occurrences. If the air is replaced by fluid and pleural thickening or eventually absorbed without operative intervention it is usually not classified as a bronchopleural fistula. Three patients had this complication resulting in large loss of function, although at the time of testing the spaces had disappeared.

Preresectional and concomitant thoracoplasties are not performed at this hospital. In the patients having lobectomies in whom there are large spaces postoperatively, which seem unlikely to be filled by the remaining lung, it is customary to perform secondary thoracoplasty about 2 weeks following the resection. Eighteen lobectomies were followed by thoracoplasties in addition to the one tabulated in Table I. The average loss of vital capacity in the thoracoplasty group was 15 per cent compared with 10 per cent for the entire group. Maximum breathing capacity data showed identical results. Seven patients had persistent large air spaces following resection and required 3½ rib thoracoplasties for closure, resulting in large loss of function. There were 2 other patients in the segmental group who required secondary thoracoplasty and their change in function was only moderate.

Atelectasis occurring postoperatively is usually handled satisfactorily by bronchoscopy. Severe atelectasis which did not clear rapidly following bronchoscopy occurred in one case of segmental resection. Atelectasis requiring thoracoplasty also occurred in one segmental case and one bilateral operation on the side of lobectomy.

Fluoroscopy revealed extensive adhesions involving the diaphragm in 3 patients with large loss of function. Four patients were noted to have paralysis of the diaphragm on the operated side diagnosed by elevation of the diaphragm and a positive sniff test seen by fluoroscopy.

Seven patients in the series have no obvious complications to account for the large combined loss of function. All were in the older age group and 3 of these were noted to have diffuse emphysema. In the patients subjected to pneumonectomy, the loss of function is due primarily to resection of functioning lung tissue. This is especially apparent when the lung is removed for scattered disease rather than for destroyed lung, as was discussed in the previous communication. Space filling thoracoplasty also causes loss of function on the contralateral side.

DISCUSSION

A number of articles have appeared in the literature regarding changes in pulmonary function following pulmonary resection since the early paper of Cournand and Berry.[2] Preoperative and postoperative values are now available for wedge resections, segmental resection, lobectomies, bilateral resections, and pneumonectomies. Only a few authors mention the importance of complications and apparently no papers are devoted primarily to complications leading to maximum loss of function.

Kraan,[3] in discussing resection in tuberculosis, draws attention to the importance of the intact diaphragm in preserving function. Phrenic avulsion or damage to the nerve during operation causing paralysis of the diaphragm may lead to marked loss of function. Van der Drift[4, 5] came to similar conclusions. The complication of activation of tuberculosis in portions of the lung not removed is cited by Kraan,[3] but in our experience this is a rare occurrence and has not greatly affected pulmonary function within 6 months after surgery. Such complications as bronchopleural fistula and empyema are frequently mentioned as causes for loss of function but these are not documented. A recent article by Björk[6] lists the following complications of segmental operations without correlating loss of function: (1) air leakage, (2) accidental opening of a tuberculous cavity, (3) wound infection, (4) ventilatory insufficiency, (5) trauma to big vessels, (6) postoperative pain, and (7) spillover with infiltration in the contralateral lung. Complications such as persistent air space, air leakage, bronchopleural fistula, atelectasis of the lung, and empyema are frequently corrected by thoracoplasty. Gaensler,[7] Lindahl,[8] and Little[9] have shown that this procedure is apt to cause a further loss of function. On the other hand, plombage for filling uninfected spaces causes a lesser diminution of function.[7, 9]

It should be emphasized that Table I does not include all the surgical complications that occurred in these 450 tuberculous patients, but only those which appeared to be associated with large loss of function. Furthermore, there were occasional deaths. Some patients severely ill from empyema or bronchopleural fistula were not available for retesting at the 6-month period. Statistics on a comparable series, including many of these patients, will be found in the Transactions of the 18th Conference of the Chemotherapy of Tuberculosis, Veterans Administration Armed Forces, 1959.

The development of postoperative paralysis of the diaphragm is worthy of special mention. In none of our 4 patients with this complication was the phrenic nerve cut or stretched at the time of operation. Great care was taken not to use the cautery to cut adhesions or control bleeding in the area traversed by the phrenic nerve. The cause for the development of paralysis remains unexplained. We have observed 1 patient, not in this series, who postoperatively had a paralysis of the diaphragm on the side opposite the operation which would seem to preclude direct injury of the phrenic nerve. That the loss of function is large, following paralysis of the diaphragm, is shown by the 4 patients in Table I; the combined loss for each was 61, 75, 57, and 56 per cent.

SUMMARY

Four hundred and fifty tuberculous patients received preoperative and postoperative pulmonary function tests. Twenty-nine patients had large losses in the vital capacity and maximum breathing capacity following operation. These cases were analyzed to determine the types of surgical complications that occurred. Intrathoracic bleeding or persistent air spaces leading to

pleural thickening and adhesions, protracted atelectasis, and impaired diaphragmatic motion were found to be often associated with a significant reduction of function Complications requiring secondary thoracoplasty also resulted in large loss of vital capacity and maximum breathing capacity In 4 patients, idiopathic paralysis of the diaphragm seemed responsible for impairment of ventilatory function

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RESULTS AND COMPLICATIONS OF PLEURECTOMY FOR BULLOUS EMPHYSEMA AND RECURRENT PNEUMOTHORAX

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SUBTOTAL excision of the parietal pleura for the treatment of recurrent pneumothorax and giant bullous emphysema has been reported by other surgeons.[1-4] We have reported our experiences in a series of patients with pneumothorax.[5] In this paper, the results and complications of pleurectomy for pneumothorax are augmented by additional patients and the results with patients treated for bullous emphysema are recorded. Between August, 1951, and June, 1958, 41 patients had 45 (4 bilateral) operations.

Of these patients, 28 were either in the military service, dependents of active duty service personnel, or were veterans who qualified for admission and treatment on the Surgical Service at Tripler U.S. Army Hospital. An additional 13 patients were seen in the thoracic surgical practice of one of us (P. W. G.). The indication for surgery was recurrent spontaneous pneumothorax in 27 instances and in the remaining 18 was bullous emphysema. The average age at the time of surgery for the patients with pneumothorax was 31 years, with a range of 19 to 71 years. For those patients with bullous emphysema the average age was 39 years at the time of surgery with a range of 28 to 70 years.

We consider subtotal parietal pleura excision the most certain method of pleural space obliteration and superior to the instillation of irritants or other open methods.

The first patient in this series was operated upon in 1951 for recurrent spontaneous pneumothorax. The second patient, for whom parietal pleurectomy was employed, submitted to staged, bilateral operations for giant bullous emphysema. The excellent result obtained in these 2 patients was encouraging and pleurectomy has since been incorporated as an important component of our surgery for these two conditions.

In addition to the obvious indication for pleurectomy, obliteration of the pleural space, a secondary gain may be realized by revascularization of the lung. Barrett and Daley[6] reported the feasibility of providing increased blood

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supply to the lung from the depleuralized chest wall for the patients with tetralogy of Fallot technically unsuitable for the Blalock or Potts operations Crenshaw and Rowles[4] attempted surgical revascularization of the atrophic degenerated lungs of emphysematous patients by this method The gross pathologic changes in the lungs of patients with spontaneous pneumothorax as seen at the operating table are remarkably similar to those observed in patients with bullous emphysema in many instances The single remarkable difference is the degree of involvement which is quite variable in any given patient We believe that spontaneous pneumothorax may be the earliest clinical expression of an atrophic, degenerative alteration of the lung parenchyma which will be recognized in later life as emphysema Therefore, if the fundamental pathophysiology of emphysema is a diminished peripheral pulmonary vascularity, progression might be prevented by early pleurectomy

The patients reported in this experience were accepted as candidates for surgery with the following indications

1 Spontaneous pneumothorax with persistent air leak (one patient)
2 Spontaneous pneumothorax with bullous lesion demonstrable by chest roentgenogram (7 patients)
3 Spontaneous pneumothorax, recurrent, unilateral, or alternating bilateral (17 patients)
4 Spontaneous pneumothorax, simultaneous bilateral (one patient)
5 Giant emphysematous bullae with progressive compression of functioning lung tissue (7 patients)
6 Giant emphysematous bullae symptomatic (8 patients)

In addition to excision of the pleura surgery included lung repair by unroofing and oversewing surface blebs and bullae with minimal sacrifice of functioning lung tissue Resection of destroyed bronchopulmonary segments or an entire lobe was necessary in only 4 of 45 operative procedures and is to be avoided as much as possible to preserve maximum function Also, resection of the pulmonary plexus of the vagus nerve was recently employed in 4 patients who had symptoms of bronchospasm in addition to pulmonary emphysema

Evaluation of postoperative results is based on observations which vary from 6 months to 6 years Three patients died either directly or indirectly as a consequence of surgery The 38 surviving patients were doing well when last seen Of the 25 patients followed after surgery for spontaneous pneumothorax, 5 have been observed for 2 and 3 years There have been no known recurrences of pneumothorax on the side of surgery Spontaneous pneumothorax of the contralateral lung has occurred in 7 patients since surgery Three of these patients had episodes of pneumothorax bilaterally, either alternating (2 patients) or simultaneous (1 patient) prior to surgery One of the patients subsequently submitted to a second operation to stabilize the second lung, others may be candidates for further surgery Of the group of patients treated for bullous emphysema, 5 have been followed 2 years or longer The postoperative observation extends 5, 5½, and 6 years, respectively, for 3 of these patients They are all symptomatically and subjectively improved In two instances pain was a primary symptom and this has been relieved

A truly objective measure of the status of these patients has not been possible because complete bronchospirometric studies were not done. Postoperative roentgenograms of the chest appear essentially normal in the majority of patients with minimal residual scarring in a few. Evaluation of preoperative and postoperative pulmonary function has been extensively investigated following surgical obliteration of the pleural space by other investigators.[1, 7] Selected patients were evaluated either because of some interesting aspect of the postoperative course, or as a long-term follow-up examination. The results of vital capacity and maximum breathing capacity measurements are presented in Fig. 1. Patient N. M. underwent right thoracotomy for giant bullous emphysema. There was little change in ventilatory function observed 2 years after surgery as compared with studies done prior to operation. The degree of intrapulmonary mixing was normal, as well as measurements of residual volume. Patient J. S. also revealed little change in ventilatory function after surgery. These studies were of particular interest because the patient had a complicated postoperative course with hemothorax, empyema, and required a delayed second thoracotomy for decortication some months after the pleurectomy which was done for bullous emphysema. Here again intrapulmonary mixing and residual volume determinations were normal and unchanged by surgery. The next patient, W. S., was operated upon for recurrent spontaneous pneumothorax with associated bullae demonstrable by chest roentgenogram. Once again there is amazingly little change noted in the postoperative measurements as compared with preoperative values. Patient J. K. submitted to pulmonary function

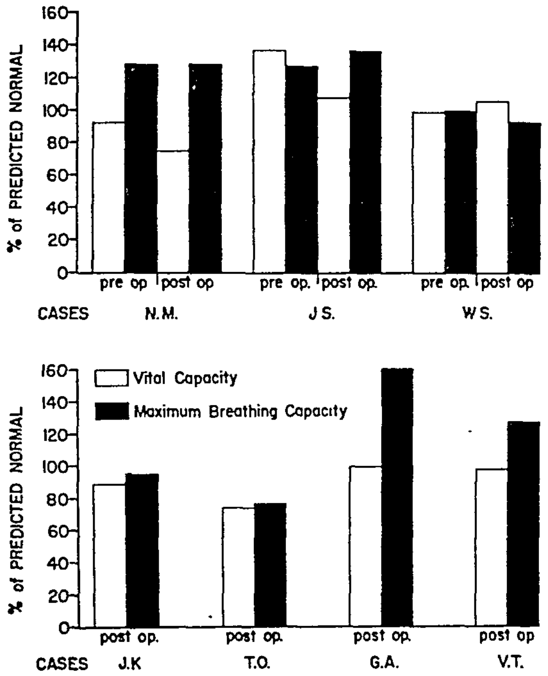

Fig. 1.—Pulmonary ventilatory function studies.

studies 6 years after bilateral surgery for giant bullous emphysema. Preoperative studies are not available for comparison. Vital capacity and maximum breathing capacity are slightly less than predicted normal values. However, this patient required resection of more lung tissue than any other in the series, the apical and posterior segments of the right upper lobe and the entire left upper lobe were removed. The next patient, T. O., was studied 5 years after bilateral surgery for giant bullous emphysema. The second operation was complicated by the development of empyema. Pulmonary function was significantly impaired in this individual. In addition to decreased vital capacity and maximum breathing capacity, the patient had paradoxical motion of the right diaphragm and increased residual air volume. The final 2 patients, G. A. and V. T., were studied approximately one year after surgery had been performed for recurrent spontaneous pneumothorax and giant bullous emphysema, respectively. The measurements are significant only in that no grossly demonstrable residual impairment is evident. Our observations of pulmonary function indicate that parietal pleurectomy, in the absence of complications, does not appear to impair the ventilatory capacity of these patients.

Some of the most important observations to be made from this series of cases concerns the complications of surgery. The operations at Tripler U.S. Army Hospital were performed for the most part by the resident staff of the surgical service. In 24 instances the operative procedures were done by one or the other of the authors, the remainder were performed under the supervision of the thoracic surgical consultant (P. W. G.). There have been 3 deaths in this group of patients since surgery, a gross mortality of 7 per cent. Two of these deaths occurred in the immediate postoperative period and one 10 weeks following surgery.

In the first case that ended fatally, surgery was undertaken in an effort to salvage a moribund patient. This individual was 71 years of age and had marked, crippling pulmonary emphysema. In addition, he had suffered repeated episodes of life-endangering pneumothoraces over the last 2½ months of life, which required intercostal catheter decompression of the pleural space and tracheostomy to prevent total respiratory collapse. He was also on digitalis for cardiac decompensation. Surgery was undertaken, with reservation, because of increasing dyspnea in spite of therapy. The patient rapidly failed after surgery in spite of mechanically assisted respiration.

The next patient was 60 years of age with marked bullous emphysema and pulmonary insufficiency. Following operation, the immediate postoperative course was uneventful and the patient was discharged from the hospital on the twelfth day after surgery. He returned to be readmitted to the hospital on the eighteenth postoperative day with signs and symptoms of acute, fulminating renal failure. This patient died within 2 days in spite of therapy and at postmortem examination a lower nephron nephrosis was observed.

The third fatal case was remarkable in that the postoperative course was complicated by many factors and extended over a 2½ month period. This patient was 37 years of age and was apparently in good health at the time of the operation. The immediate postoperative course was complicated by hemorrhage of moderate severity over a period of 5 days. Blood loss was not massive during this time but the patient required transfusions daily. Subsequently, the patient recovered slowly to become asymptomatic with the exception of a slight exertional dyspnea. Repeated thoracenteses were done but all residual air pockets and blood could not be removed from the pleural cavity. The patient was allowed to return home to be followed at frequent intervals as an outpatient. Successive chest roentgenograms showed progression of the pneumothorax space and increased pleural reaction. The patient was readmitted 2 months following surgery for elective decortication of the lung. However, because of increasing dyspnea, anemia, and subsequent fever while in the hospital, surgery was withheld. Thoracentesis yielded purulent material. Within several days, fresh bleeding was detected within the pleural space, coincident with the development of a shower of cutaneous petechiae. Within a very short time, ecchymoses, and gastrointestinal hemorrhage developed and the patient became comatose and died. Postmortem examination confirmed the terminal clinical picture of thrombocytopenic purpura of undetermined origin. In retrospect, the initial postoperative hemorrhage was probably an unrecognized manifestation of the abnormality although the patient had a normal bleeding and clotting time prior to operation.

Any discussion of parietal pleurectomy always stimulates a question as to the amount of blood lost from the large denuded area of the chest wall. With the exception of the case just cited this has been a contributing factor in the increased morbidity of one additional patient only. This individual required 3,500 c.c. of whole blood transfusion during and after surgery. He developed a hemothorax which became secondarily infected. The patient subsequently submitted to a secondary thoracotomy and decortication. Pulmonary function studies one year later revealed little change (Fig. 1, Patient J. S.) as compared with those done prior to surgery. The blood replacement was tabulated and found to vary between 500 to 3,500 c.c. per patient, excluding the patient with thrombocytopenia who required well over 10,000 c.c. during the postoperative period up to his death. The average blood replacement during and following surgery, therefore, was 1,300 c.c. In only 5 instances was more than 2,000 c.c. of blood replacement required. The amount of blood replacement following complete parietal pleurectomy is comparable to that amount of blood necessary following most intrathoracic surgical procedures, and is not considered excessive. From this experience, it would be wise to consider all possible conditions which might contribute to hemorrhage in the postoperative period before accepting pleurectomy as the responsible factor in any given patient with excessive bleeding.

The complications encountered in this series of patients have been tabulated (Table I). It is interesting to note that the minor complications occurred primarily in the patients treated for pneumothorax as opposed to the group of patients operated upon for bullous emphysema in whom the major complications predominated. Any postoperative air leak beyond 5 days was considered persistent. The longest period of postoperative air leak was 10 days; all subsided with continued intercostal catheter drainage. Similarly, any residual air space discernible by chest roentgenogram after removal of the thoracotomy drainage tubes was recorded as a residual pneumothorax. *All residual air spaces resolved spontaneously, usually within a short period* of time. The longest time required for resolution was 4 months in one patient. Contralateral spontaneous pneumothorax was recorded as a complication only if it occurred during the postoperative period of hospitalization. In only one instance was this sufficiently severe to require treatment. The major complications, with the exception of the single episode of atelectasis, occurred in the group of patients treated for bullous emphysema. This is, in part, a reflection of the older age of these patients as well as the more extensive pulmonary disease present at the time of surgery. The eight major complications recorded were encountered in 5 patients following 5 operative procedures. Several of these have been discussed at some length. In addition to the patient with hemothorax who developed empyema, infection occurred in one additional patient following the second of staged bilateral operations. This was treated successfully by repeated aspiration and chemotherapy. Pulmonary function studies 6 years later in this patient (T. O.) revealed some impairment of ventilatory capacity as previously noted (Fig. 1). One patient returned to the hospital on the thirteenth postoperative day, after being discharged, with a small, aspiration-type lung abscess in the left lower lobe. A good therapeutic response to chemotherapy was obtained, with complete resolution in 7 days.

TABLE I. COMPLICATIONS OF SURGERY

COMPLICATIONS	NO. CASES
Minor	
1. Persistent air leak	3
2. Residual pneumothorax	3
3. Contralateral pneumothorax	3
Major	
1. Hemorrhage	2
2. Empyema	2
3. Atelectasis	1
4. Lung abscess	1
5. Lower nephron nephrosis	1
6. Thrombocytopenia, idiopathic	1

DISCUSSION

Partial parietal pleurectomy has a definite place as a method of obliterating the pleural space in patients requiring surgery for spontaneous pneumothorax and giant bullous emphysema. The immediate results following surgery have been gratifying in this series of patients. Several patients have now been followed 5 to 6 years without evidence of progression of lung bullae of a size sufficient to be discernible by chest roentgenogram. It is possible that the additional increase in blood supply provided to the lung surface by this procedure will be of lasting benefit. In the absence of severe complications there is no indication that pulmonary function is jeopardized by this operation. The mortality following operation was not directly the result of pleurectomy although surgery was a contributing factor in each instance. If one continues to accept elderly debilitated patients with pulmonary insufficiency as candidates for surgery, this will be a deterring feature. Postoperative bleeding is not usually a major feature; however, when it does occur, it should not be too hastily attributed to pleurectomy lest one overlook other possible causes of hemorrhage. The usual blood loss associated with pleurectomy is comparable to that of other intrathoracic operations and has not been excessive.

The total incidence of postoperative complication was 38 per cent of 45 operations including 3 fatalities: Minor complications which did not influence or prolong morbidity constituted over one half of the total or an incidence of 20 per cent. In only one instance was a complication of surgery responsible for residual impairment of pulmonary function. Major complications, which included hemorrhage, empyema, atelectasis, and lung abscess, occurred in 5 of 38 surviving patients who submitted to 42 operative procedures, an incidence of 12 per cent. The high rate of surgical complications in this series should serve to caution those individuals who would recommend simultaneous bilateral surgery for patients with recurrent spontaneous pneumothorax as has been advocated.[2]

Although the pathologic changes may be bilateral in a significant number of patients with spontaneous pneumothorax, only 7 of 26 patients have had clinically detectable pneumothorax of the contralateral lung since operation. This might have been anticipated in 3 patients who had episodes of contralateral pneumothorax prior to surgery. On the other hand, 2 patients who had contralateral pneumothorax at some time prior to surgery have not had recurrence since surgery. Therefore, only 25 to 35 per cent of patients requiring thoracotomy for recurrent pneumothorax will have bilateral difficulties. Of these, not all will subsequently require a second operation. If all patients are subjected to simultaneous bilateral surgery, the larger percentage will have a needless or meddlesome operative procedure. The increased risk associated with such an undertaking does not seem to be justifiable at the present time.

SUMMARY

The following observations have been made from this series of 41 patients who submitted to 45 thoracic surgical procedures which included partial parietal pleurectomy as an important component of the operation. Pleurectomy will obliterate the pleural space and in addition may provide a desirable increase in blood supply to the peripheral lung tissue. Postoperative results are excellent in patients now observed up to 6 years following surgery. A significant mortality may be anticipated following surgery of this nature performed on individuals with marked pulmonary insufficiency or among those in older age groups Postoperative bleeding of alarming magnitude should not be hastily attributed to the raw pleural surface without first considering the possibility of rupture of a major blood vessel or some defect in the blood clotting mechanism as a causative factor The incidence of surgical complications is of such magnitude and seriousness as to discourage any ill conceived idea that simultaneous bilateral surgery of this nature is not fraught with great risk to the patient

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SUPERIOR VENA CAVAL REPLACEMENT WITH SPONGE TEFLON PROSTHESIS

A Preliminary Report

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THE MANAGEMENT of superior vena caval obstruction has remained a singularly perplexing problem to the internist and vascular surgeon alike. The literature review of McIntire and Sykes,[1] published in 1949, contained 524 cases of superior vena caval obstruction. In 1952, Veal and Cotsonas[2] reported their experience with sixty-one obstructions which involved either the superior vena cava or the innominate veins. The 61 cases in their series had been seen over a 15-year period at one institution. Failor, Edwards, and Hodgson[3] recently reviewed 33 necropsy cases of superior vena caval obstruction, all of which had been seen at the Mayo Clinic. Allansmith and Richards[4] reported, from a single institution, a series of 21 cases of superior vena caval obstruction in which attempts at surgical alleviation had been undertaken. The above-mentioned reviews indicate that superior vena caval obstruction is not an infrequently occurring entity.

Primary malignant thoracic tumors are unquestionably the most common etiologic factor underlying superior vena caval obstruction.[1, 3] However, in 17 of the 21 surgically treated cases reported by Allansmith and Richards,[4] the underlying etiologic lesion was noted to be of a benign nature. The incidence of chronic fibrous mediastinitis as a primary etiologic factor in superior caval obstruction has been variously reported as 12 to 15 per cent.[1, 3] The latter lesion has an exceedingly poor ultimate prognosis if left untreated. It, therefore, behooves us to seek and develop a satisfactory means of surgical management for superior vena caval obstruction secondary to a benign causative factor. A consideration of the underlying disease process seemingly makes bypass or actual resection and replacement of the involved caval segment, perhaps, the most logical, as well as feasible, surgical procedure.

Numerous procedures have been devised and applied experimentally and, on occasion, clinically. Atriocaval anastomosis, described by Gerbode and associates[5] in 1949, and the use of a pedicle tube created from the right atrium and atrial appendage, described by Riberi and Moore,[6] have both been reported

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as successful procedures when applied experimentally Neither of these procedures appealed to us when considering the technical problems of their clinical application since they are both limited with respect to the length of superior vena cava which can be replaced Autogenous aorta has also been used experimentally for superior vena caval replacement with a high incidence of success by Moore and Riberi The magnitude of such a procedure, and its probably significant associated morbidity and mortality, has discouraged us from consideration of this procedure as clinically applicable

Deterling and Bhonslay[8] utilized autogenous venous tissue, enlarged through the panel technique, as a means of experimental superior vena caval replacement but found its use attended with a high incidence of failure Aorta homografts and various synthetic prostheses have been applied experimentally[8, 9] and have also been found to be unsuitable as venous substitutes Allansmith and Richards[4] reported various clinical successes with the use of arterial homografts and heterografts, venous autografts, and a crimped nylon prosthesis They neglected to report the duration of follow up in their cases and stated that some of the grafts were thought to have become obstructed after several months

In spite of the above mentioned reports of failure attending the use of synthetic vascular prostheses in superior vena caval replacement, they seemed to us to be the most appealing logical, feasible, and applicable surgical procedure Such a procedure is obviously dependent upon the development and utilization of a synthetic material whose physical and chemical properties have minimal associated host reaction and a high incidence of success as a vascular substitute

We feel that these characteristics are inherently embodied in Teflon which, to date, has enjoyed considerable success as a vascular prosthesis in aortic and arterial replacement and bypass procedures The purpose of this report is to present our experience with the use of porous sponge Teflon, constructed in the form of a vascular prosthesis, and its evaluation in experimental superior vena caval replacement

MATERIALS AND METHODS

Healthy mongrel dogs, weighing 17 to 30 kilograms, were used in this study Anesthesia was induced with intravenous Nembutal in a dose of 30 mg per kilogram of body weight Respiration was maintained with the aid of a cuffed endotracheal tube, and a mechanical respirator utilizing alternately positive and negative pressure

In all animals, a right thoracotomy was performed through the right third intercostal space The vena cava was dissected free from its attachment to the right atrium to include the right and left innominate veins The right innominate vein was ligated and divided to allow excision of as long a segment of vena cava as possible The length and circumference of the segment of vena cava to be excised were measured A graft of slightly larger dimensions was constructed from a ⅛ inch thick sheet of porous sponge Teflon. The longitudinal seam of the graft was doubly sewn with an over-and-over suture of 3-0 vascular silk in such a manner that the sutures were not visible within the lumen of the graft. That segment of the vena cava extending from just distal to the left innominate vein to just proximal to the azygos vein was excised and replaced with the previously constructed prosthesis of porous sponge Teflon. A single row of over-and-over 5-0 vascular silk sutures was used for both anastomoses. Vena caval occlusion during the period of resection and anastomosis was maintained by the use of atraumatic curved clamps. The period of vena caval occlusion varied from 28 to 33 minutes. At the completion of the procedure, the graft was not covered with pleura (Fig. 1). The chest wall was closed in layers and a catheter was left in the right pleural space for 24 hours for aspiration of air and drainage material. Penicillin was given the day of and the day subsequent to operation.

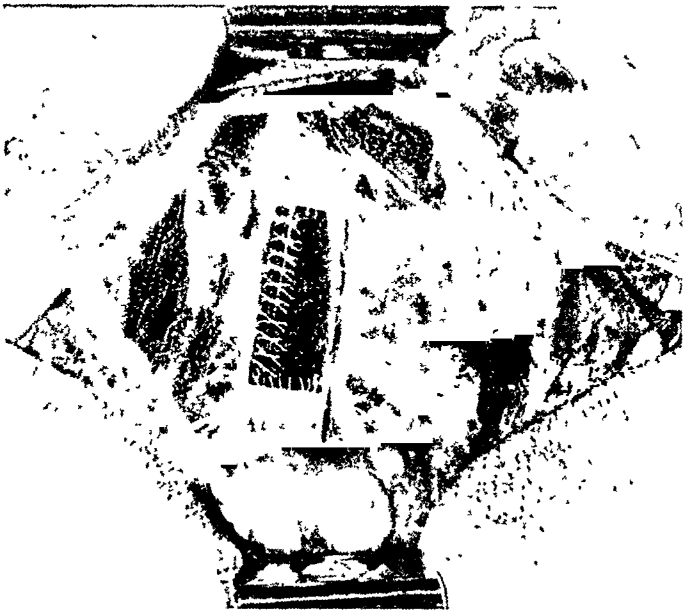

Fig. 1.—Porous sponge Teflon prosthesis replacing the superior vena cava. Longitudinal seam of constructed graft readily apparent. Phrenic nerve along left side of graft.

RESULTS

The operation of superior vena caval replacement with a prosthesis constructed from a sheet of porous sponge Teflon was carried out as described in 20 dogs. Maintained patency of the prostheses was determined in all animals by superior vena cava angiogram, autopsy, or both, from 1 week to 6 months following operation.

Four animals died at periods of 1 week to 2 months following the operative procedure. Atelectasis was the apparent cause of death in a single animal which succumbed 1 week following operation. Autopsy in this case revealed a patent graft. A second animal died apparently from affects secondary to occlusion of the graft as determined at the time of autopsy. A third animal succumbed to a respiratory infection and autopsy in this case revealed a patent graft. The cause of death in the last animal was not apparent at the time of postmortem examination and the graft in this case was also found to be patent.

Superior vena cava angiograms were performed on 16 animals. Twelve of the grafts were found to be patent for varying periods of 1 to 6 months (Fig. 2). Four of the prostheses were noted to be occluded and this finding was substantiated by subsequent animal sacrifice and autopsy. In 2 animals, although definite patency of the grafts was established, there was noted to be a narrowed *segment within the graft. The latter animals have remained healthy and will* ultimately undergo further evaluation to determine duration of graft patency and host reaction to the porous sponge Teflon prostheses. A single animal was sacrificed 2½ months following operation to corroborate findings of patency, as previously determined by superior vena cava angiogram, and to allow gross and histologic evaluation of the fate of the prosthesis and the associated host tissue reaction. In this latter case, a widely patent functioning graft was found (Fig. 3). Eleven animals with patent grafts remain well and will be maintained to allow ultimate long-term studies of duration of graft patency and gross and histologic host tissue reaction.

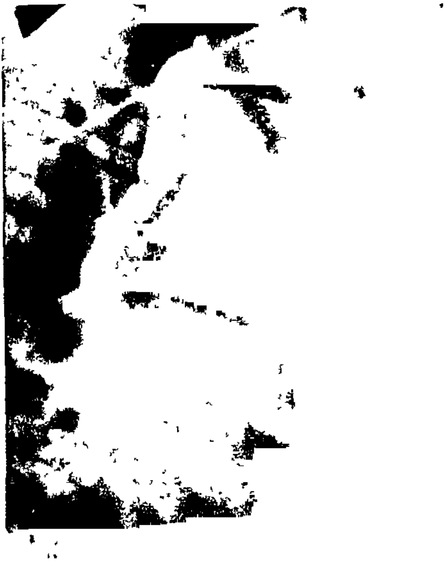

Fig 2—Superior vena cava angiogram of an animal 4 months following insertion of porous sponge Teflon graft in the superior vena cava. Widely patent graft apparent with good *visualization of right auricle and ventricle*

Graft patency, then, was maintained, as determined by superior vena cava angiogram and/or postmortem examination, in 15 of the 20 animals in the study for a maintained patency percentage of 75 per cent.

The appearance of the graft lumen in the 4 animals who died or were sacrificed and had patent grafts varied with the duration of time subsequent to the operative procedure. The lumen of the graft obtained 1 week following surgery was noted to be lined with an adherent, fibrinous coagulum approximately 2 mm. in thickness (Fig. 4). The lumens of the grafts examined 2 weeks following surgery had a similar adherent, fibrinous lining, which in areas appeared to be less than 2 mm. in thickness as though the lining was undergoing a process of resorption in those scattered areas. The lumen of the graft examined 2½ months subsequent to surgery was noted to have a

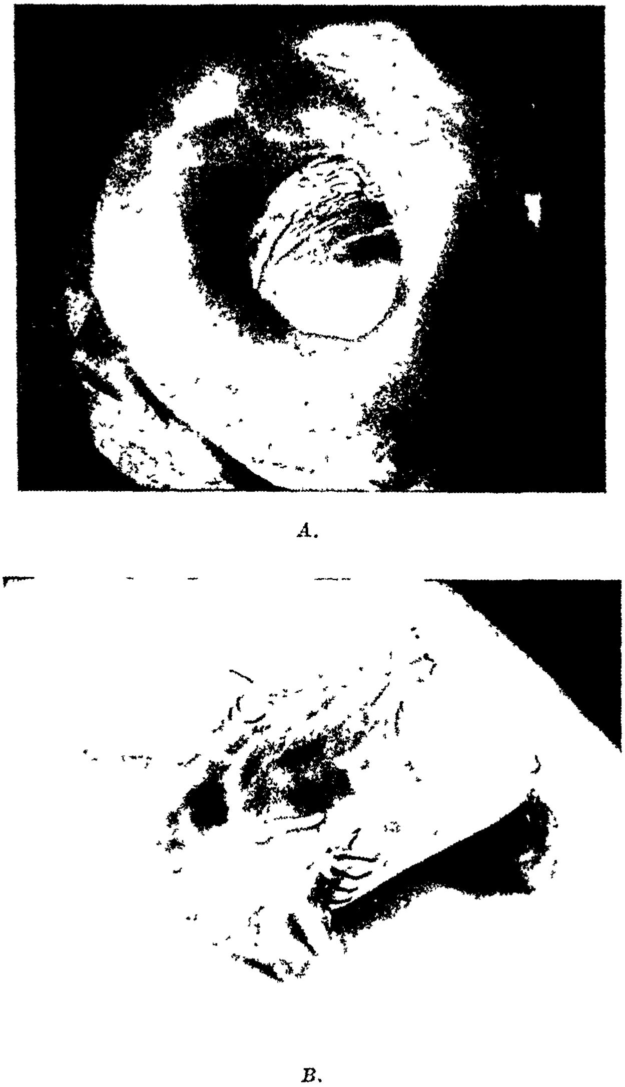

Fig. 3.—Sponge Teflon superior vena caval prosthesis removed from animal 2½ months following surgery. *A* shows graft on end with everted segment of vena cava and smooth lining of graft. *B* shows same graft opened with smooth lining at sites of anastomosis and within the graft lumen.

smooth, shiny, thin lining as though completely endothelized (Fig. 3). The suture lines in all four patent grafts examined were well healed as early as 1 week following surgery (Fig. 4).

Postmortem examinations performed on animals, after a period of a month or greater had transpired since surgery, revealed densely adherent fibrous tissue reactions about the grafts. Although the fibrous tissue about the graft could be stripped from the external surface, it appeared to be intimately adherent as though invading the graft proper. Histologic studies of canine host reaction to implanted porous sponge Teflon, carried out prior to and in conjunction with this study, revealed to us that the sponge Teflon is actually invaded by host fibroblastic reaction and is well incorporated into the body by the host fibrous tissue reaction. A more detailed description of canine host tissue response to implanted porous sponge Teflon will appear in a subsequent report.[10]

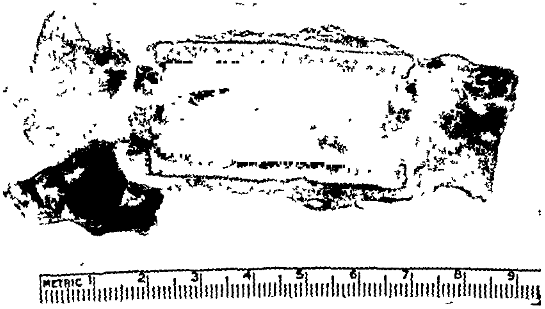

Fig 4—Porous sponge Teflon prosthesis removed from animal one week following surgery The graft was patent and functioning Thin adherent fibrinous coagulum is seen lining the graft lumen Good healing seen at sites of anastomosis

DISCUSSION

Certain features inherent in synthetic vascular prosthesis which make them highly desirable are worthy of review. Among these are their ready availability in varying sizes. The sponge Teflon used in this study was obtained in flat sheets, ⅛ inch thick, which were malleable enough to allow construction of varying sized tubes. The grafts, as we constructed them, were admittedly somewhat crude and of necessity contained a longitudinal seam. Due to the fact that the material was ⅛ inch thick, we were, with some practice, ultimately able to construct a prosthesis without the suture material presenting within the lumen of the graft. We hoped that this would lessen the chance of initiating clot formation at the site of the longitudinal seam. Seamless tubes of the same material in varying sizes would obviously be more desirable than our somewhat crudely constructed grafts.

A highly desirable characteristic of Teflon is the fact that it may be autoclaved without significant alteration of its physical properties. To ensure asepsis, all of the Teflon used in these experiments was autoclaved prior to construction and implantation of the prostheses. The physical characteristics of the sponge Teflon, in the thickness used, allowed a significant degree of firmness of the grafts and prevented collapse of the implanted prostheses, an obviously desirable feature when considering the problems of a vascular substitute for replacement in such a low pressure system as the vena cava. A graft which is easily collapsible in a low pressure system, or readily compressible by a normal fibrotic tissue response, has obvious liabilities as a venous substitute and was therefore avoided.

The excellent experimental and clinical results of others with the use of Teflon prostheses as arterial substitutes appeared to us an additional reason for experimenting with its use in the venous system. Although we were initially concerned with the host reaction to Teflon in the sponge form, implantation studies, previously alluded to, revealed to us that the material would, in fact, ultimately be invaded by host fibroblasts and be incorporated within the host fibrous tissue reaction. The porous sponge Teflon contains interconnected spaces which allow growth of fibroblastic tissue into and ultimately completely through the prosthesis, a factor apparently necessary in any synthetic material if it is to be accepted by the host as a vascular substitute. The incidence of successful vena caval replacement with a synthetic substitute, which was achieved in these studies, stands in sharp contrast to the rather high incidence of failure with the use of other synthetic prostheses similarly employed and previously reported by others.[8] Although excellent results have reportedly accompanied the experimental use of fresh autogenous aorta as a vena caval replacement, its use entails a far more formidable procedure than the use of a readily available synthetic prosthesis. If, then, similarly excellent results can be obtained with the synthetic prosthesis, it would seem to be the more desirable procedure.

We are cognizant of the fact that our prostheses have been evaluated for periods of only up to 6 months following surgery but we feel that the results achieved, to date, with the rather crudely constructed grafts, justify this report.

Last, the incidence of the maintained patency of 75 per cent of the porous sponge Teflon prostheses, which was achieved in these canine studies, makes the use of similar Teflon prostheses as venous substitutes worthy of more detailed and extensive investigations. Such studies are currently under way in our laboratories.

SUMMARY

The experimental use of porous sponge Teflon protheses for superior vena caval replacement in canine animals has been presented. The results obtained, as reported herein, justify more extensive investigative amplification. If the results achieved in these studies are maintained in long-term evaluation studies, the clinical utilization of porous sponge Teflon as a superior vena caval prosthesis is indicated.

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OPERATION OF THE ROLLER PUMP FOR EXTRACORPOREAL CIRCULATION

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The Kay-Cross rotating disc oxygenator has now been used in over 250 operative procedures. It has proved itself to be a safe, simple, and efficient method of oxygenating blood. Over 150 cardiac centers where this oxygenator is employed, either clinically or experimentally, have substantiated this view. The development of convoluted discs increases the gas exchange surface by 40 per cent over the flat surface discs.[1]

Two different types of pumping systems have been used in conjunction with the Kay-Cross disc oxygenator in this hospital. Sigmamotor pumps were used initially and performed quite satisfactorily. However, laboratory studies on pump output, arterial line pressure, hemolysis, and perfusion led to the use of the Pemco type of De Bakey roller pumps. These pumps have been used in the last 100 patients with what is considered to be a marked improvement in perfusion management. The hemodynamic aspects of this pumping mechanism are reported in this paper, and the principles used in carrying out perfusion pumping are stated.

DESCRIPTION OF THE PEMCO ROLLER PUMP

The Pemco roller pump† in its present form is shown in Fig. 1. A system of rollers compress a rubber latex pump chamber over a 200 degree arc with a circumferential distance of 11 inches. No valves are used. A manual variable speed control ranges between 0 to 80 r.p.m. The distance of each roller from the pumping tract can be adjusted by a small screw which alters its center of rotation in relation to the roller arm and thus its distance from the tract. The roller system may be removed from the central pump shaft and systems containing two, three, and four rollers inserted into the pump. (Fig. 2). The rubber latex pump chamber may be varied in size for optimum stroke volume and flow rate.

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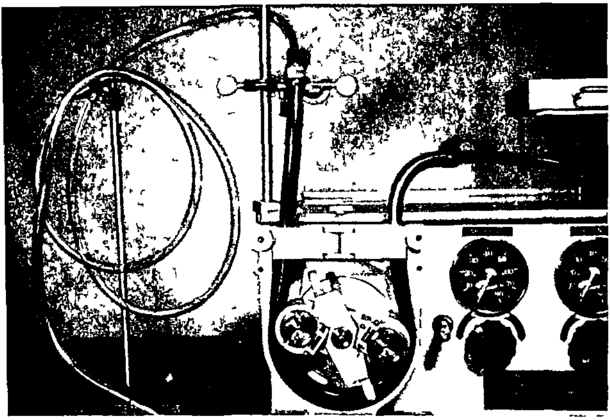
†Manufactured by Pemco, Inc., 5663 Brecksville Rd., Cleveland 31, Ohio.

Tygon tubing is used to connect the pump chamber to the arterial cannula and to the oxygenator. A 3 foot length of 1/2 inch internal diameter tubing is used to the oxygenator, a 7 foot length of ⅜ inch internal diameter tubing to the arterial cannula The arterial cannulae are 3 1/2 inches long. Each consists of a stainless steel connector and Teflon tubing The American wire gauge numbering system is used in referring to cannula size.

Fig. 1



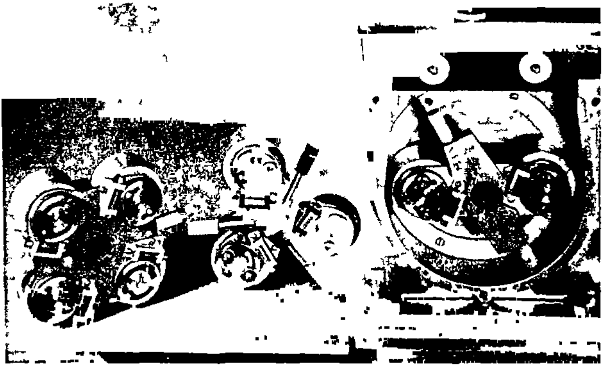


Fig 2

Fig 1 —The Pemco roller pump with adjustable rollers rubber latex pump chamber, 14 inch extension as depulsator, Tygon tubing and the arterial cannula

Fig 2 —The two three and four roller systems

LABORATORY STUDIES

Each of the variable aspects of the pumping system, i e , the roller setting, the number of rollers, the chamber size, and the cannula size was studied in regard to the manner in which its alteration alone affected: (1) pump speed, flow rate, and arterial line pressure; (2) blood damage as indicated by hemolysis; and (3) perfusion of the patient as indicated by arterial pressure, flow, and vascular resistance.

METHODS

1. *Pump Calibration.*—Calibration of flow was done with blood at room temperature with the arterial cannula directed into a graduated cylinder 36 inches above the oxygenator reservoir. Flow per minute was determined at intervals of 10 r.p.m. Stroke volume was calculated as flow divided by revolutions per minute times the number of rollers in the system.

2. *Arterial Line Pressure.*—A No. 18 needle connected to a Statham transducer, which recorded on a Sanborn 150 recorder, was directed against the blood flow in the output end of the rubber latex pump chamber. This is the point of maximum pressure in the pump system. The resistance to flow at this point results from the Tygon connecting tubing, the cannula size and length, and the hydrostatic pressure equal to the distance between the blood reservoir and the tip of the arterial cannula in the graduated cylinder.

3. *Hemolysis.*—This is expressed as the change in the level of plasma hemoglobin with each passage of blood through the pump. Plasma hemoglobin was determined by a modification of the method of Hunter.[2] The recirculating system used to analyze the role of the pump in the production of hemolysis was the same in every way as that used during perfusion except that the rotating discs were left out of the oxygenator and no sump suction was fed into the system. In this way, the resulting hemolysis reflected only that produced by the pumping mechanism. Studies carried out with the discs in place and rotating indicate that there was no significant detectable damage to the blood from this source. In order to eliminate differences in red cell fragility and hematocrit, each series of tests were run from the same pool of blood. Fresh dog blood, anticoagulated with heparin, was used in 1,500 c.c. aliquots for each test run. Ten cubic centimeter samples of blood were taken from the arterial end of the oxygenator bottle at 15-minute intervals for runs of from 1 to 3 hours. The total hemolysis for each run was calculated as the difference in plasma hemoglobin in milligrams per cent, from the beginning of the run to the end. The hemolysis per blood passage was calculated from the flow rate, the circulating pool size, and expressed as milligrams per cent plasma hemoglobin.

4. *Perfusion Studies.*—Adult mongrel dogs, anesthetized with intravenous pentobarbital and anticoagulated with heparin, were perfused with the heart-lung machine. The arterial cannula was placed in the femoral artery. Venous blood was returned to the oxygenator through cannulae in each vena cava connected directly to the venous pump. Perfusion is controlled by maintaining a constant blood level in the oxygenator, and a normal venous pressure in the superior vena cava. This is correlated in conjunction with the appearance of the conjunctival vessels to maintain a constant blood volume and normal

blood pressure in the patient. In all instances, where the effects of the pump on perfusion were being determined, the heart was open and empty so that its action could not affect the perfusion. Aortic pressures were recorded from a catheter inserted into the abdominal aorta through the femoral artery. Pressure in the arterial line was taken in the tubing near the arterial cannula. The gradient across the arterial cannula was calculated as the difference between the mean arterial line pressure and the mean aortic pressure. In calculating the gradient across the animal's vascular system, the right auricular pressure was considered to be zero, the resistance of the vascular system being expressed as the ratio of the pressure gradient between the aorta and the right auricle to the calculated flow rate.

For clinical perfusions, the variable aspects of the pumping system must be adjusted to produce the flow rate selected for the individual. This and the size of the arterial cannula used are largely determined by the patient's weight and the caliber of the superficial femoral artery. Since both these factors are relatively fixed for each patient, the data on pump performance are presented from this standpoint, that is, to produce a given flow rate through a specific cannula.

RESULTS

Tables I, II, III, and IV present the data obtained from the studies on pump hemodynamics. These are self explanatory.

By tightly occluding the rollers, the amount of blood destruction per passage through the pump is increased (Table I). By adjusting the rollers to be nonocclusive, the large back flow through the pump decreases the stroke volume to the extent that excessively rapid pump speeds are necessary to produce a sufficient flow rate. With this setting, the affect of the resistance in the perfused subject markedly changes the calculated flow of the pump.

TABLE I. THE EFFECT OF ROLLER SETTING ON FLOW RATE, PUMP SPEED, ARTERIAL LINE PRESSURE, FLOW REDUCTION WITH RESISTANCE, AND HEMOLYSIS USING THE TWO ROLLER PEMCO PUMP WITH A ¾ INCH I.D. CHAMBER AND A NO. 10 ARTERIAL CANNULA

ROLLER SETTING	NONOCCLUSIVE*	JUST NONOCCLUSIVE†	TIGHT OCCLUSIVE‡
Flow (c.c./min.)	2,000	2,000	2,000
Pump speed (r.p.m.)	50	23	21
Stroke volume (c.c.)	20	42	48
Arterial line pressure (mm. Hg)	410/240	400/200	420/180
Pulse pressure (mm. Hg)	170	200	240
Decrease in flow at 36 in. hydrostatic pressure	200	100	0
Hemolysis in mg. % per passage	0.045	0.054	0.090

*Nonocclusive setting = 300 c.c./min. back flow at 36 in. hydrostatic pressure.
†Just nonocclusive setting = no back flow at 36 in. hydrostatic pressure.
‡Tight occlusive setting = no back flow at any arterial line pressure.

Therefore, the just nonocclusive setting, by compromising between these two settings, decreases hemolysis and permits only a small back flow. This is the roller setting used in all of the pump studies. Because of this just nonocclusive roller setting, the pump must be calibrated against a simulated resistance, and there is a loss in stroke volume with an increase in the arterial line pressure (Table II).

TABLE II. THE EFFECT OF PUMP SPEED AND CANNULA SIZE ON STROKE VOLUME WITH THE JUST NONOCCLUSIVE SETTING OF THE ROLLERS

	STROKE VOLUME	
R.P.M.	CANNULA NO. 6 (C.C.)	CANNULA NO. 10 (C.C.)
10	66	39
20	53	32
30	55	31
40	53	31
50	49	30
60	48	30
70	47	29
80	47	28

The addition of rollers to the pumping system (Table III) shortens the effective pumping tract and decreases the stroke volume without decreasing the distance that each roller must travel during the pump cycle. Therefore, hemolysis is markedly increased. The addition of four rollers to the pumping system extends the speed range of the pump from 160 to 320 strokes per minute, without significantly increasing the flow rate. When the stroke volume is reduced by adding rollers, a given flow can be pumped with a lower pump speed in revolutions per minute than when the same flow rate is pumped using fewer rollers.

TABLE III. THE EFFECT OF ROLLER NUMBER AND CHAMBER SIZE ON ARTERIAL LINE PRESSURE, PUMP SPEED, STROKE VOLUME, PULSE PRESSURE, AND HEMOLYSIS WHEN PUMPING 2,000 C.C./MINUTE THROUGH A NO. 10 ARTERIAL CANNULA WITH THE PEMCO ROLLER PUMP SET TO BE JUST NONOCCLUSIVE FOR BLOOD

Roller number	2	4	2	2
Chamber size in inches I.D.	½	½	¾	⅜
Flow (c.c./min.)	2,000	2,000	2,000	2,000
Pump speed (r.p.m.)	33	41	24	76
Stroke volume (c.c.)	30	12	42	13
Arterial line pressure (mm. Hg)	390/190	410/150	400/200	420/200
Pulse pressure (mm. Hg)	200	260	200	220
Hemolysis in mg. % per passage	0.40	1.0	0.06	0.50

The configuration of the pulse pressure curve within the pump is influenced by the length of the pump tract (Fig. 3, *A*). By lengthening the tract, the ejection of the stroke volume is prolonged and the maximum pressure and flow sustained over a larger portion of the pump cycle. This is in contrast to the action of the heart wherein the major portion of the stroke volume is ejected in one tenth of the cycle.

Decreasing the size of the pump chamber decreases the stroke volume, but necessitates an increase in pump speed from 24 to 76 r.p.m. in order to maintain the flow rate (Table III). This limits the flow range at which the smaller stroke volumes can be used. By enlarging the chamber, the flow range of the pump is extended. The hemolysis produced by the 3/8 inch pump chamber is significantly less than that seen when an equal reduction in stroke volume is produced by the four roller system (Table III).

Enlarging the internal diameter of the arterial cannula, either by using two vessels of the same size or placing it in a single larger vessel, significantly lowers the arterial line pressure at which a given flow is reached (Table IV). This lowering of pressure and, thus, pressure gradient across the arterial cannula, is not, however, associated with a significant decrease in the level of hemolysis

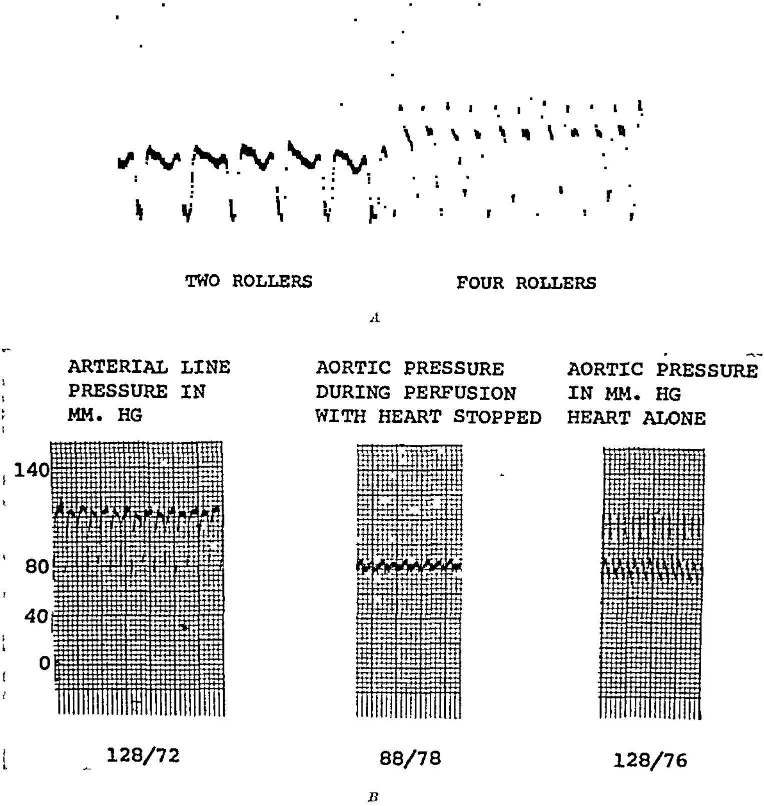


Fig 3—*A*, Arterial line pulse pressure curves using the Pemco two and four roller systems

B, Arterial line and aortic pressure curves during perfusion with a two roller Pemco pump ⅜ inch I D chamber and No 10 cannula compared to aortic pressure curve with the heart alone

The significant factor responsible for hemolysis from the pump is the compression of the pump chamber by occlusive rollers (Tables I, III, IV, and V). Stroke volume affects hemolysis only as it influences pump speed The pressure gradient across the arterial cannula does play some role in blood damage, but quantitatively this is small. The absolute level of the arterial line pressure has no influence on hemolysis (Table V).

TABLE IV. THE EFFECT OF CANNULA SIZE AND NUMBER ON PUMP SPEED, STROKE VOLUME, ARTERIAL LINE PRESSURE, PULSE PRESSURE, AND HEMOLYSIS WHEN PUMPING 2,500 C.C./MINUTE WITH A ⅝ INCH PUMP CHAMBER OF A TWO ROLLER PEMCO PUMP

Cannula size	No. 10	No. 6	No. 10 (2)
Flow (c.c./min.)	2,500	2,500	2,500
Pump speed (r.p.m.)	39	31	22
Stroke volume (c.c.)	32	40	57
Arterial line pressure (mm. Hg)	600/390	230/30	170/40
Pulse pressure (mm. Hg)	210	200	130
Hemolysis in mg. % per blood passage	0.4	0.3	0.4

TABLE V. COMPARISON OF PUMP SPEED AND ARTERIAL LINE PRESSURE IN THE PRODUCTION OF BLOOD DAMAGE EXPRESSED AS PLASMA HEMOGLOBIN IN MG. % RESULTING FROM THE CIRCULATION OF BLOOD THROUGH THE PEMCO ROLLER PUMP SET TO BE JUST NONOCCLUSIVE FOR BLOOD

Roller number	2	2	4	4	2	2
Pump speed	20	60	20	60	60	60
Arterial line pressure	—	—	—	—	272/112	640/440
Cannula size	None	None	None	None	6	10
Priming volume	1,500	1,500	1,500	1,500	1,500	1,500
Length of run (min.)	60	60	60	60	60	60
Flow per minute (c.c.)	1,675	4,440	1,190	3,366	3,950	2,360
Total blood passage	67	172	42	130	130	81
Total hemolysis	32	66	33	141	37	33
Total hemolysis per blood passage in mg. %	0.48	0.4	0.79	1.0	0.3	0.4

The effects of the roller type of pump on the hemodynamics within the blood stream of the perfused subject is presented in Tables VI, VII, and VIII.

The level of aortic pressure during perfusion is related to the flow rate as long as the quantity of blood in the perfused subject remains constant (Table VI). However, the relationship between flow and aortic pressure is not a linear one, the higher flow rates being associated with a decreased effect on blood pressure. In the normal individual, this, in all probability, is a result of the moderator reflexes originating from the carotid sinus and tending to maintain a constant arterial pressure over a wide range of cardiac outputs.[3] In situations encountered during open heart surgery, where abnormally large quantities of blood are returned to the heart chambers via the coronary sinus, bronchial arteries, or incompetent aortic valve, this relationship does not hold. Under these circumstances, the rate of flow has little effect upon the level of aortic pressure beyond a certain point.

TABLE VI. THE EFFECT OF FLOW RATE ON PULSE PRESSURE, MEAN AORTIC PRESSURE, AND VASCULAR RESISTANCE IN A 16 KG. DOG USING A 3 ROLLER PUMP WITH A ½ INCH CHAMBER AND A NO. 10 CANNULA

Cubic centimeters per kilogram	50	75	90	170
Cubic centimeters per minute	820	1,230	1,470	2,800
Pump speed (r.p.m.)	15	25	32	60
Stroke volume (c.c.)	18	16	15	15
Mean aortic pressure	60	70	80	100
Aortic pulse pressure	8	8	8	4
Vascular resistance (mean pressure/flow)	0.07	0.06	0.05	0.04

The pulsations within the aorta are considerably dampened when compared to those in the pump lines and in the blood stream when perfusion is carried on by the heart action (Table VII) This depulsated flow produced by the roller type of pump results mainly from the continuous nature of its pumping action The duration of time during the pump cycle that the rollers are not functioning is short This brief period is that in which the pressure fluctuations occur (Fig 3, *B*) The width of the pulse pressure in the aorta is also affected by the stroke volume and the pressure gradient across the arterial cannula (Tables VII, VIII) Increasing the stroke volume from 17 to 70 c c doubles the pulse pressure in the aorta

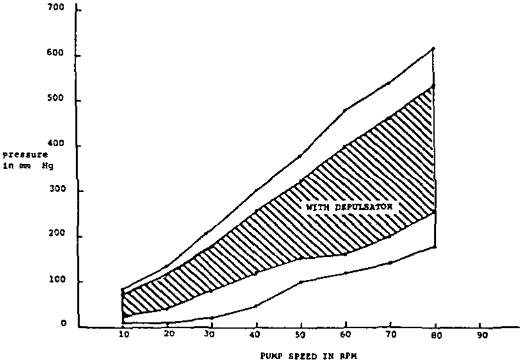


Fig 4 —Arterial line pressure with and without a 14 inch depulsator

Table VII The Effect of Stroke Volume on Pump Speed, Arterial Line Pressure, Aortic Pressure and the Aortic Pulse Pressure When Flowing 700 c c Per Minute Through a No 9 Cannula Using the Roller Pump and the Sigmamotor Pump

Pump type and chamber	2 roller 3/8 in	2 roller 3/4 in	Sigmamotor 3/8 in
Flow (c c /min)	700	700	700
Pump speed (r p m)	20	5	114
Stroke volume	17	70	6
Arterial line pressure (mm Hg)	168/100	168/108	168/64
Aortic pressure (mm Hg)	120/108	128/104	72/60
Aortic pulse pressure (mm Hg)	12	24	12

Table VIII The Effect of Pressure Gradient on Flow Rate, Pump Speed, Stroke Volume, Aortic Pressure, and Aortic Pulse Pressure Using a 2 Roller Pemco Pump With a ⅜ Inch Chamber and No 9 and No 12 Arterial Cannulae

Cannula number	9	12
Flow (c c /min)	1,050	1,050
Pump speed (r p m)	30	40
Stroke volume (c c)	18	13
Arterial line pressure (mm Hg)	208/80	780/380
Aortic pressure (mm Hg)	72/60	108/88
Aortic pulse pressure (mm Hg)	12	20

The pressure fluctuations within the pump tubing reflect the differences in elasticity between it and the blood vessels. Here in the pump tubing the pulse pressure increases as the arterial line pressure rises and the tubing becomes inelastic. The elasticity in the pump assemble can be increased by extending the rubber latex pump chamber from 7 to 14 inches beyond the pump output head (see Fig. 1). This decreases the line pulsations by lowering the systolic pressure and raising the diastolic. There is no change in flow rate, mean line pressure, or hemolysis resulting from this rubber depulsator (Fig. 4).

DISCUSSION

From these studies it is apparent that the Pemco roller pump is capable of producing a pump flow with a variety of characteristics. The range of stroke volume may be adjusted between 3 and 70 c.c. The number of strokes per minute can be controlled between 0 to 320. The rollers can be adjusted so as to control the back flow through the pump. The pulsatile characteristics of the flow may be controlled by adjusting the elasticity of the pump tubing and the level of pressure gradient across the arterial cannula. This range of adaptability makes the pump suitable for incorporation into any system of extracorporeal circulation. It allows the characteristic of the pump flow to be regulated, within limits, to incorporate a variety of perfusion concepts.

The method of perfusion control developed for the Kay-Cross disc oxygenator, as used during the past 250 operative cases, has been outlined under methods of perfusion. The following method of pump assembly has been found to facilitate the operation of this perfusion. It has lowered the level of hemolysis resulting from cardiac bypass with the pump oxygenator. It has not been associated with any detectable disadvantages.

1. *Hemolysis.*—Three considerations have been employed to reduce blood damage. The rollers are not tightened to completely occlude the pump chamber. The three and four roller systems are not used. The speed of the pump during perfusion has been reduced by adjusting the stroke volume of the pump.

2. *Flow Characteristics.*—A flow as nonpulsatile as possible is used both through the patient and the extracorporeal system. This is done by not using large stroke volumes or high pressure gradients. Small stroke volumes are also avoided, since the associated increase in pump speed raises hemolysis. Rubber latex depulsator tubing is used on both the arterial and venous pumps as a means of further decreasing the pulsatile characteristics of the flow occurring from the use of intermediate stroke volumes.

3. *Pump Speed.*—All patients are perfused in the same range of pump speed, between 30 to 60 r.p.m. This is done by correlating the size of the pump chamber with the arterial cannula to be used so that the stroke volume of the pump will be such that a pump speed of 40 r.p.m. will produce a flow rate of 75 c.c. per kilogram per minute. This places what may be considered the patient's resting cardiac output in the center of the pump speed range at a pump speed equal to the normal heart rate, 80 beats per minute.

This maneuver calibrates the pump speed range to fit the patient being perfused It allows flow rates up to 170 c c per kilogram per minute to be administered to the patient by adjusting the pump speed

4 *Pressure Gradient*—A single arterial cannula placed into the femoral artery through the superficial femoral artery is used in all instances The safety of the pump connections has been considered to be the major factor in adjusting the pressure gradient across the arterial cannula If the maximum pressure in the arterial line is below 500 mm Hg, it is believed to be in a safe range if the connections are properly fixed There is no major advantage to be gained from the standpoint of hemolysis or flow rate by maintaining the lowest possible pressure gradient between the pump and the patient

With the pump speed calibrated to fit the patient, the pump speed approximately that of the heart rate, and a nonpulsatile flow, the perfusion is smoothly controlled A steady flow from the venous cannulae, a smooth surface of the oxygenator blood level, and a small pulse pressure in the ascending aorta[6] are all considered to be advantageous characteristics obtained from this type of pump operation

A comparison of similar groups of patients perfused for the repair of ventricular septal defects with the Sigmamotor pumps and with the Pemco type of roller pumps, indicates that the total level of hemolysis has decreased from an average of 88 mg per cent to 44 mg per cent

It should be kept in mind that this type of perfusion does not exactly reproduce the pumping action of the heart[4, 5] Reproduction of the cardiac action during perfusion, although more physiologic from a theoretical point of view, would present serious disadvantages when used with an extracorporeal oxygenating system and method of perfusion dependent to some extent on nonpulsatile flow As there have been no detrimental effects of this type of perfusion on the patient, it is felt that there is little to be gained in modifying the pump to be less continuous The unavoidable existence of a pressure gradient between the pump and the patient, the advantages of a nonpulsatile type of flow from the standpoint of oxygenator function, and the desirability of eliminating large pressure fluctuations in the aorta while the left auricle is open,[6] all contribute to the suitability of a continuous flow pump in this type of extracorporeal circulation

SUMMARY

Hemodynamic studies on the Pemco type of De Bakey roller pump indicates that it can be adjusted to operate occlusively or nonocclusively The speed of the rollers can be increased so as to produce up to 320 strokes of the rollers per minute The stroke volume can be varied between 3 to 70 c c Elongation of the pump chamber increases the elasticity in the pump tubing and acts as a depulsator

The major factor responsible for hemolysis due to the pump is the compression of the pump chamber by occlusive rollers and the number of strokes per minute to produce a given flow The multiple roller system containing three and four rollers, although extending the speed range of the pump, significantly increases hemolysis. The level of the pressure gradient and the size of the stroke volume have little quantitative role in blood damage.

A method of pump operation wherein the pump is calibrated to fit the cardiac output range of the patient, the pump speed approximately that of the heart rate, and the flow of a nonpulsatile quality, has been found to produce little hemolysis, to be easily controlled, and to work well with the Kay-Cross disc oxygenator.

This type of perfusion has been used in over 100 operative cases. It has lowered hemolysis without changing the nonpulsatile characteristics of the flow.

We wish to express our appreciation to Dr. Matthew Levy, Director, Department of Research, St. Vincent Charity Hospital; Andre Lux, Clinton Blazek, and Janet Osborn for technical assistance, and to Harry Macko, medical technologist, for chemical analysis of plasma hemoglobin.

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VACUUM REGULATOR FOR CARDIOTOMY RETURN AND CHEST DRAINAGE SYSTEMS

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THE USUAL method of regulating the amount of suction applied to the cardiotomy return system during open heart surgery or to the pleural cavity following cardiopulmonary surgery is governed by the submergence of an open end glass tube below the water or mercury level in a container subjected to a source of suction [1, 2] In order to increase the amount of suction, the depth of submergence is increased, a plastic tube at the end of the air vent is occluded or several bottles are placed in series Often the resultant vacuum is not known Encumbrance of the setup, breakage of the containers or air vent tube, spillage of water and mercury, and leaks around the fittings or the corks are additional factors which justify the construction of a small, inexpensive, simple, durable, and accurate vacuum regulator †

DESCRIPTION AND PERFORMANCE OF VACUUM REGULATOR

Fig 1 shows the external appearance of the regulator and Fig 2 the details of its construction It is about 9 cm in diameter and 13 cm in height It has a central knob that indicates, in centimeters of mercury, the amount of vacuum that will be held The knob applies a force through an Inconel‡ spring to a seat disc which reacts to the vacuum and regulates the amount of room air admitted into the line connecting the source of suction to the container The resultant vacuum is maintained close to the setting of the knob (Fig 5) The vacuum range of the regulator is a function of the inner spring At present, the range is from 0 to 10 cm of mercury, marked in centimeter graduations Fig 3 demonstrates the position of the regulator in the cardiotomy return system during open heart surgery and Fig 4 in pleural drainage Fig 5 depicts the pressure flow characteristics of the vacuum regulator

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‡This low stressed corrosion resistant spring should not require replacement or recalibration

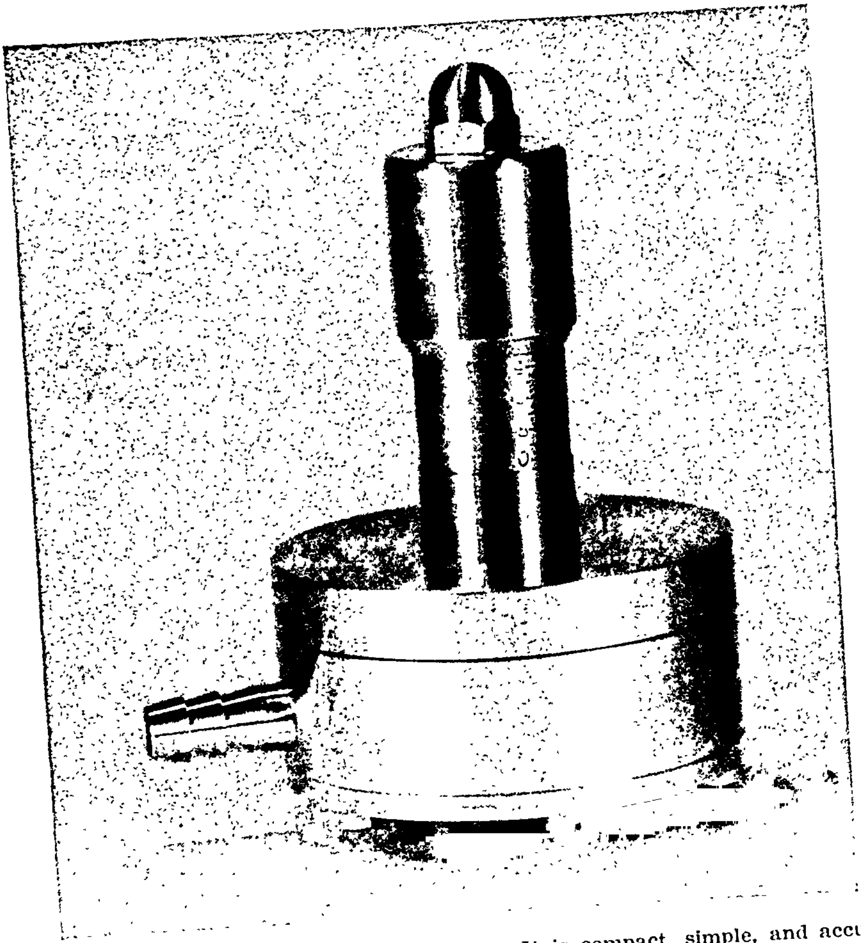

Fig. 1.—External appearance of vacuum regulator. It is compact, simple, and accurate. Calibrations are in centimeters of mercury.

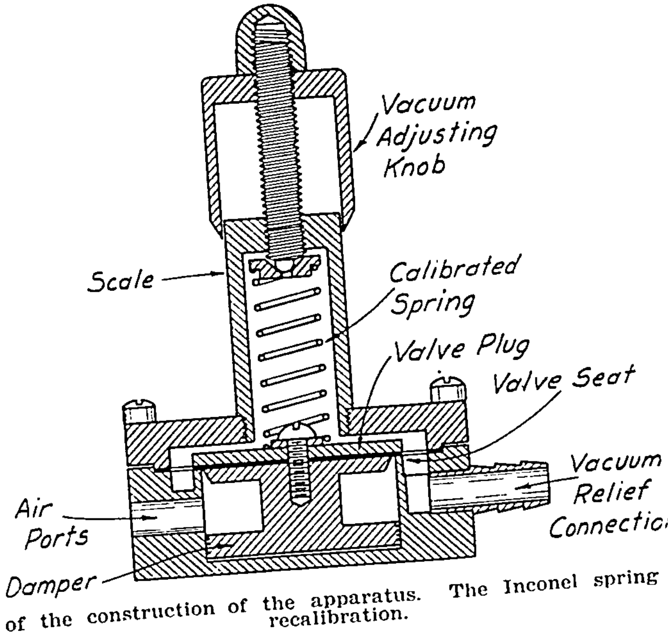

Fig. 2.—Details of the construction of the apparatus. The Inconel spring does not requi recalibration.

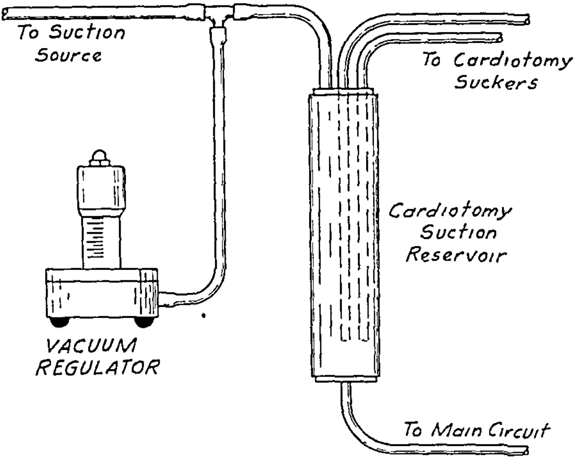

Fig 3—Position of vacuum regulator in cardiotomy return Readiness and simplicity are major features

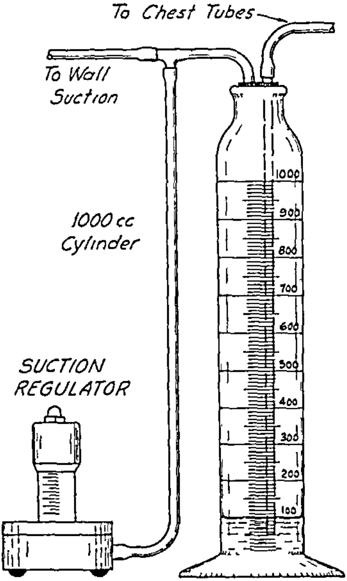

Fig 4—Position of regulator in pleural drainage Accurate measurements of blood loss are feasible and vacuum pressure changes instantly accomplished

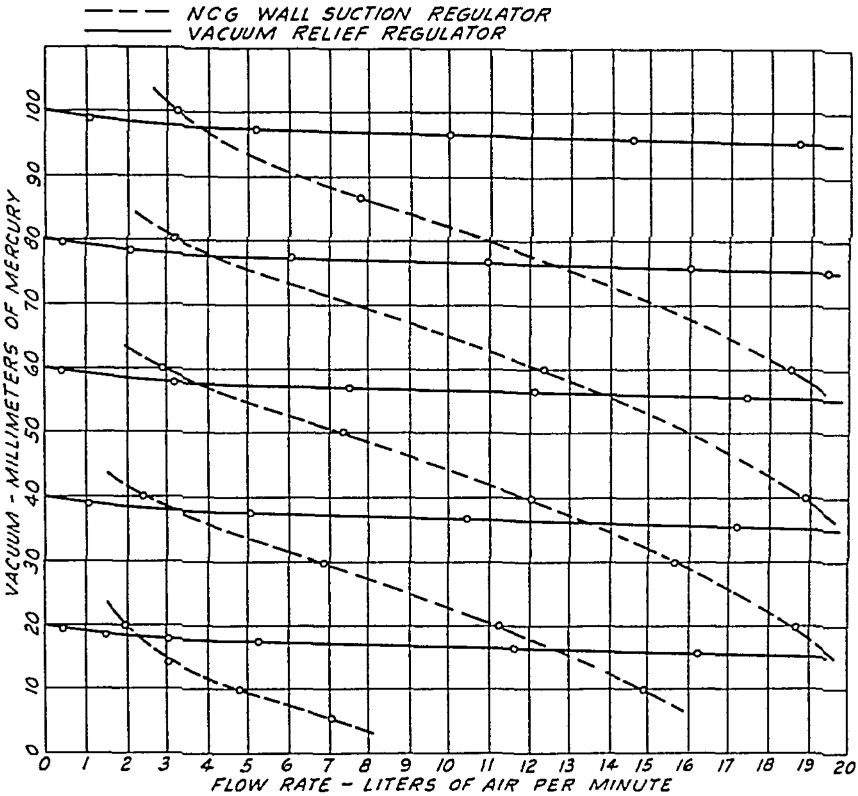

Fig. 5.—Flow-pressure characteristics of vacuum regulator up to 20 L. per minute are shown together with the control characteristics of wall suction installation (NCG 238-50V). Vacuum pressure changes of only 0.5 cm. Hg occur with air flow rates from close to 0 to 20 L. per minute.

CONCLUSION

A vacuum regulator is described for the cardiotomy return and pleural cavity drainage system. It is small in size, dependable, unbreakable, and the vacuum applied is known and maintained at all times.

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THE DESIGN OF MONITORING DEVICES FOR USE WITH A PUMP-OXYGENATOR

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THERE HAS been much discussion, since the use of extracorporeal circulation became widespread, about the principles of perfusion that will give optimal results. In this hospital the problem has been approached, not on the basis of high or low flows but by attempting to maintain the blood gas relationships within normal limits. It is felt that if sufficient oxygenated blood is provided by a pump oxygenator to maintain a reasonable perfusion pressure, and if the quantity and rate of delivery of oxygenated blood results in a normal arterial-venous oxygen difference, then adequate perfusion has been attained. The actual amount of blood perfused in cubic centimeters per kilogram per minute varies from patient to patient, but as judged by the oxygen consumption of the patient and the adequacy with which this consumption is met, the perfusion is adequate.

In order that perfusions may be conducted according to these principles, monitoring devices have been introduced into the extracorporeal circuit. It is necessary to monitor simultaneously and continuously arterial and venous oxygen tensions and arterial pH in the machine. In addition, in the patient, mean arterial and venous pressures, electroencephelogram, temperature, and electrocardiogram are also measured. The arterial oxygen tension and the pump speed determine the disc speed required. At a given pump speed, the greater the disc speed the greater the degree of oxygenation obtained. The pump speed is determined by the perfusion pressure, the venous oxygen tension and the electroencephalogram. A small arterial-venous oxygen difference is taken to mean overperfusion and too large an arterial-venous oxygen difference indicates underperfusion.

Control of carbon dioxide tension in arterial blood as estimated by pH is acomplished by altering the per cent carbon dioxide in the gas "respired" in the oxygenator. Two gas mixtures of oxygen and carbon dioxide containing 2 per cent and 4 per cent, respectively, are used. A total flow of about

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12 L. per minute is satisfactory and, by varying the proportions of each mixture, the percentage of carbon dioxide can be altered and, thus, the pH maintained within normal limits.

The pH is measured by a Beckman Zeromatic meter which reads continuously and has a self-correcting device actuated every second. It is accurate to within plus or minus 0.05 pH and is thoroughly reliable and simple to operate. At the start of each perfusion, a sample of pump blood is taken off and its pH read on a Beckman Model G meter and the calibration of the Zeromatic meter is thereby checked.

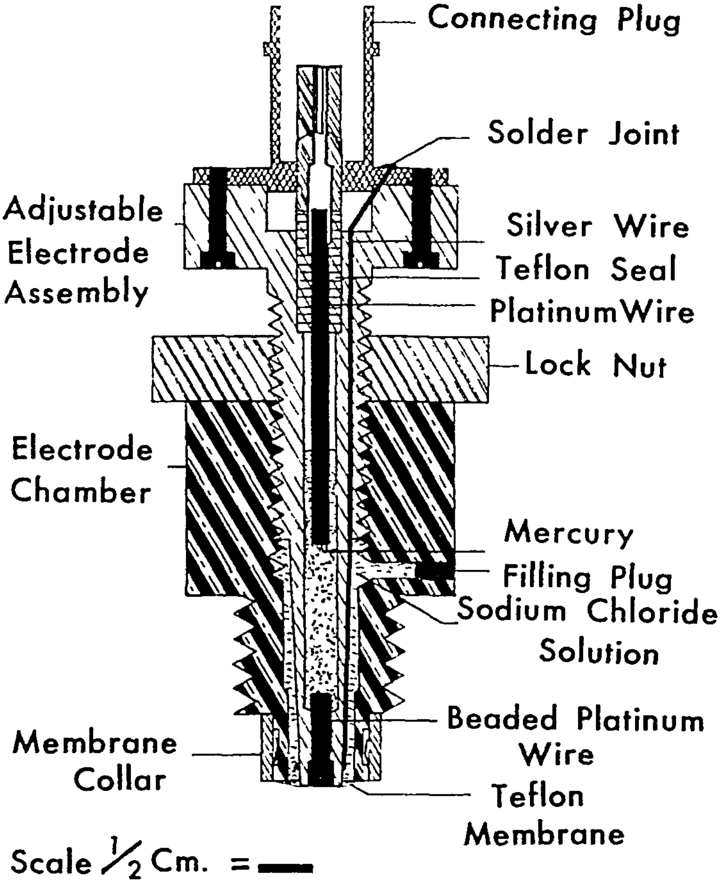

Fig. 1.—Membrane-covered polarograph.

The need for continuous monitoring of pO_2 necessitated the design of special electrodes (Fig. 1). The electrodes used are modifications of the Clark[1] polarograph. The electrode unit is in two parts; an inner core containing the electrodes and an outer chamber enclosing the electrode assembly. The platinum electrode lies in the center of the core and is divided at its middle. The separated ends dip into a sealed pool of mercury and in this way electrical contact is maintained while the differences between the coefficients of expansion of Teflon and platinum are eliminated. The silver electrode lies along the outside of the core and its tip encircles the Teflon rod. A Teflon membrane, 0.002 inch thick and 0.5 inch in diameter, is held in place over the end of the electrode chamber by a removable collar.

The use of Teflon rather than other plastics permits the electrode to be autoclaved. This is done with the electrode disassembled. To reassemble the unit, the membrane is first secured in position and the electrode chamber filled with normal saline solution. During filling, a small screw plug is removed from the side of the chamber through which air bubbles may escape while the electrode assembly is being screwed into position. When the tip of the platinum electrode is sufficiently advanced beyond the end of the chamber to make the membrane tense and slightly tented, the lock nut on the assembly is tightened. No further change can then occur in the position of the electrode tip.

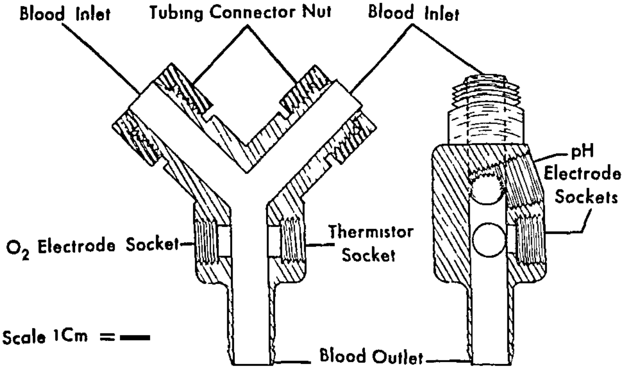

Fig. 2.—Multi electrode adaptor

The polarographs are connected with circuit control units so calibrated as to register oxygen tensions directly. The circuit used in this unit is similar to that described by Severinghaus and Bradley,[2] but has been modified to deliver a potential difference of 0.7 volt across the electrodes.

Under both experimental and clinical conditions, these polarographs have been found to react almost instantly to changes in oxygen tension, but are not so sensitive as to be difficult to control. They are not affected by changes in temperature or pressure in the blood but slight changes occur in the readings with variations in blood flow rates.

In order to introduce these electrodes into the circuit, special adaptors have been designed to house them (Fig. 2). At the venous end, the adaptor consists of a simple tube with a side hole into which the polarograph is screwed. This adaptor also has another attachment to which a short circuiting tube from the arterial end of the circuit for use during the period of equilibration before perfusion may be attached. At the arterial end the adaptor is more complicated and is located between the outflow tube from the oxygenating cylinder and the arterial pump. It consists of a Y junction rejoining the blood flows from the two oxygenating cylinders and in the sides of which are screw plugs containing a polarograph, thermistor, and two pH meter electrodes. The dimensions of the adaptor are given in Table I.

TABLE I

	VENOUS ADAPTOR	ARTERIAL ADAPTOR
Length	5 $^{15}/_{16}$ in.	3 $^{7}/_{8}$ in.
External diameter	1 $^{9}/_{16}$ in.	1 in.
Internal diameter	$^{5}/_{8}$ in.	$^{1}/_{2}$ in.

SUMMARY

The principles of perfusion used at the University of Colorado and the consequent need for continuous monitoring devices have been described. A plea is made for attempting to achieve "physiologic" perfusion.

Details are given of an autoclavable polarograph and multi-electrode adaptor for the continuous monitoring of extracorporeal perfusion.

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THE PREVENTION OF HEART BLOCK IN THE SURGICAL REPAIR OF INTERVENTRICULAR SEPTAL DEFECT

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HEART BLOCK is reported to be an important cause of morbidity and mortality following surgical correction of interventricular septal defect.[1-3] If this complication were eliminated, operative risk in most cases would then be minimal and surgery could justifiably be recommended for less seriously ill patients. In this way, many individuals could enjoy full activity and normal growth and development which they otherwise would be denied.

Current figures, if they were available, would undoubtedly show that this complication is encountered less frequently now because of the improvements in perfusion methods and operative technique. However, the incidence is still significant.[3] When heart block occurs its management is greatly facilitated by the myocardial electrode and electronic pacemaker,[9] but in those patients who have persistence of complete atrioventricular block, cardiac function may be seriously compromised. They are prone also to sudden death.

Heart block has not occurred in our series of 53 cases of interventricular septal defect. The surgical technique to be described seems to have eliminated the problem of heart block while providing a reliable method for obtaining complete closure of each type of defect.

SELECTION OF PATIENTS

Initially, only those patients with pulmonary hypertension were accepted for operation. As our experience increased and operative risk was shown to be minimal in the less severe cases, the criteria for selection were liberalized. At present, in addition to the pulmonary hypertensive group, those patients who have evidence of large left to right shunts are also advised to have operation. The minimal operative mortality and morbidity in these cases has justified this decision.

PATCH DESIGN

A satisfactory technique should provide secure closure of the septal defect irrespective of its size and location or the characteristics of the surrounding

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septal tissue. It must consistently avoid injury to the conduction system of the heart. Because an actual tissue deficit is present, a substitute plastic patch material would seem desirable. This is particularly true in the larger defect or in those in which the septal rim is thin. If no patch is employed, tension on the sutures, with ensuing edema and punctate hemorrhage, increases the likelihood of conduction disturbances. Also, disruption of the repair under the stresses of heart contraction might occur.

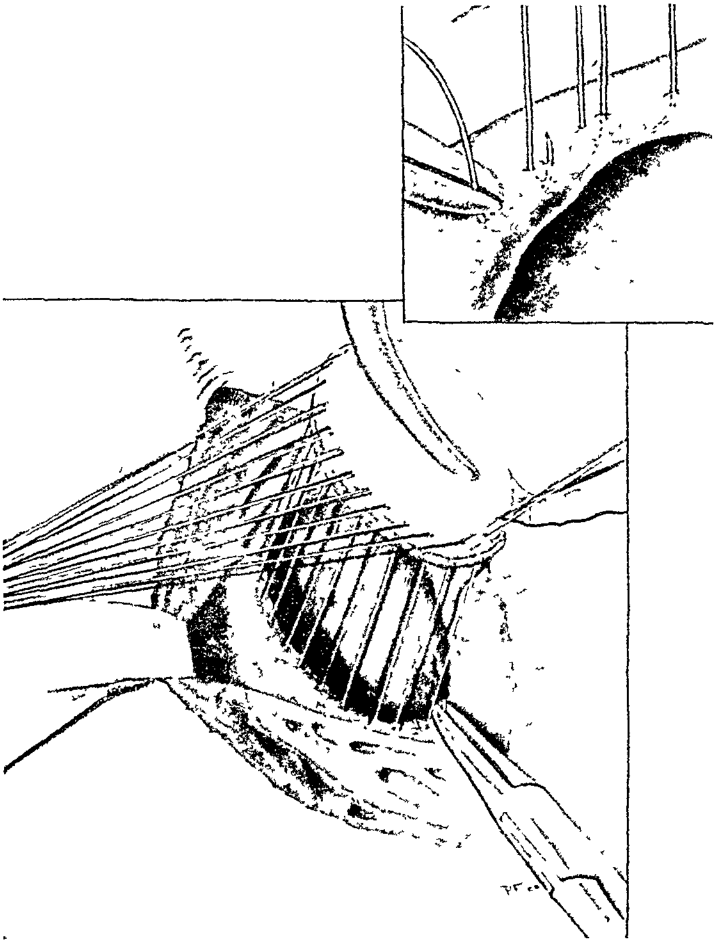

Fig. 1—This drawing shows the two-component patch being used to close a large defect. The overlapping of the sutures is shown The noncompressed polyvinyl sponge lies against the septum; the Teflon felt faces the cavity of the right ventricle The *inset* illustrates the method of placing the Mersilene sutures in the rim of the defect so that they lie parallel to the course of the conduction fibers. Note the slight overlapping of the mattress sutures.

The danger of incorporating the conduction fibers in the sutures being placed in the posterior rim of the defect has been adequately emphasized.[1, 8, 10] However, because these pathways lie just beneath the endocardium,[1] they may easily be traumatized if they are pressed against a hard, semirigid patch material when the sutures are tied down. This is particularly true when the white fibrous tissue is absent from the posterior rim, and the edge of the patch must lie against the muscle containing these fibers. The possible role of injury from patch compression has not been sufficiently stressed.

The plastic cloth patch that has proved to be most satisfactory consists of two components. They are: polyvinyl (Ivalon) sponge and Teflon felt.* The Ivalon sponge is 2 mm. thick and is not compressed. It provides the desired cushion effect and applies itself evenly to the contours of the septal rim. The Teflon felt is 2 mm. thick and faces the cavity of the right ventricle (Fig. 1). It holds sutures well; it is flexible and provides the needed strength for the patch. Thus, a firm repair of the larger defects is obtained without having to tighten the sutures excessively and risk crushing the septum. Usually two or three sizes are prepared prior to starting the bypass. They are held in readiness in a tonsil hemostat.

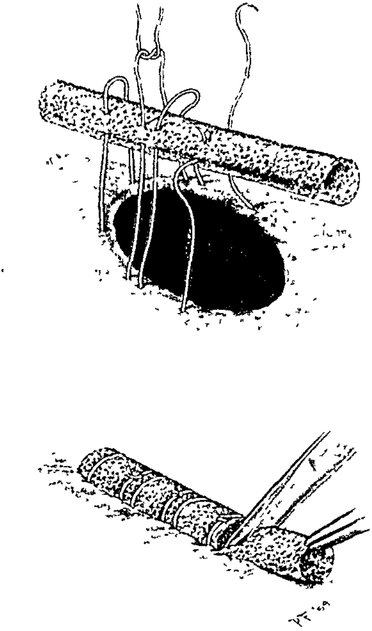

Fig. 2—This drawing illustrates the use of a noncompressed cigaret-shaped polyvinyl sponge to close smaller defects with firm fibrous rims.

For defects around 1 cm. in size with strong fibrous rims, an alternate patch material has been used. This consists of a cigarette-shaped piece of noncompressed polyvinyl sponge (Fig. 2). It is prepared with cork borers in two sizes, ¼ inch and ⅜ inch in diameter.

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*Available from Mr. Norman C. Jeckel, United States Catheter and Instrument Corp., Glens Falls, N. Y.

As an additional precautionary measure, Mersilene* sutures have been employed routinely for all septal suturing during the past year because of their smoother surface and low tissue reactivity. These are double-armed with sturdy small needles excellently suited for work in this crowded area.

OPERATION

A mechanical heart-lung apparatus of the Kay-Cross type was employed in all cases. Potassium citrate arrest was used routinely. A vertical sternotomy is now used exclusively except in those patients with an associated patent ductus arteriosus.

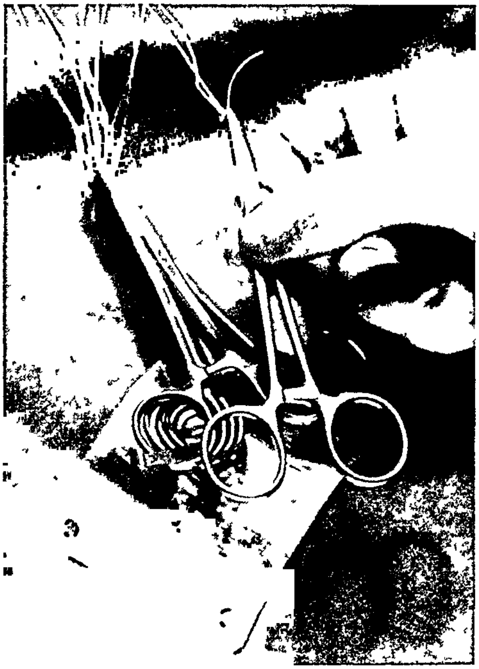

Fig. 3.—This photograph demonstrates the hemostat holder which keeps each successive suture in sequence, thereby preventing entanglement. Two are used, one for each side of the septal rim.

Technique.—

1. *Large defects over 1 cm. in diameter or those with thin rims:* A series of 3-0 atraumatic Mersilene sutures are placed mattress-fashion around and parallel to the rim of the defect so that each suture slightly overlaps the preceding suture (Fig. 1). In this way, the course of the needle through the tissue and the imbedded suture itself always lies parallel to the course of the conduction fibers. The first suture is placed in the anterosuperior angle of the defect. After the suture is placed in the septum, the two ends are separately passed about 3 mm. from the edge through both layers of the patch being held by the assistant in a tonsil hemostat. A patch which is large enough to allow a 2 to 3 mm. overlap at the edges is chosen. The suture ends are held together in a

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*Mersilene sutures are Du Pont's Dacron polyester fiber. Supplied in 24 inch lengths with 2 RB-1 needles by Mr. C. W. Norman, Ethicon, Inc., Somerville, N. J.

hemostat, the needles are cut off, and the hemostat is placed in a special hemostat-holding bracket located at each side of the operative field (Fig. 3). These brackets keep the hemostats in order and prevent later entanglement and confusion while the patch is being tied in place. The subsequent sutures are placed counterclockwise proceeding along the posterior rim of the margin of the defect toward the postero-inferior angle. Full-thickness sutures are placed in the white fibrous tissue if it appears strong. If the posterior rim of the defect appears thin, the sutures are placed in the adjacent muscle. Here, a more superficial bite is taken, but a broader area of tissue is incorporated in the mattress suture. At the postero-inferior angle, the suture is placed as close to the edge of the septum as possible. The remainder of the sutures are then placed along the anterior rim, proceeding from the postero-inferior angle to the starting point. This part of the septum is usually muscular and is away from the conduction fibers. Deeper sutures should be taken to obtain secure closure. The patch is then put in place with the tonsil hemostat, and the sutures are tied down in reverse order of their insertion. Just before the last one is tied, the left ventricle is compressed with the hand to express entrapped air bubbles Each suture is cut about 1 to 2 mm. from the knot.

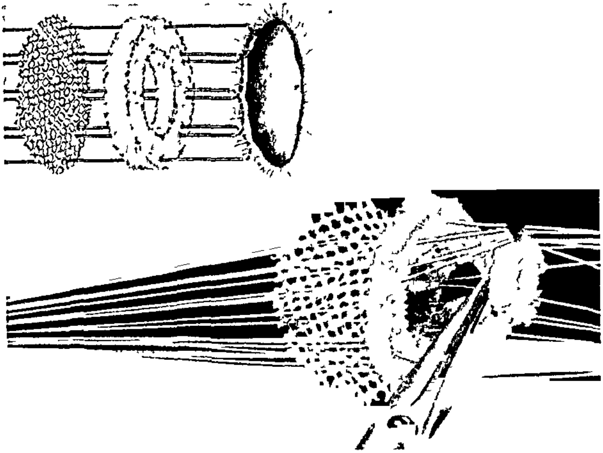

Fig 4 —This illustration shows the modified septal patch for cases with severe pulmonary hypertension due to high vascular resistance The cushion effect of the polyvinyl sponge is retained and the mesh permits gradual obliteration of the shunt

In the presence of high pulmonary vascular resistance, the patch is modified to permit gradual closure; in such patients, a Teflon cloth mesh* is substituted for the Teflon felt. The central portion of the polyvinyl sponge is excised (Fig. 4) leaving a rim of compressible sponge lying against the septum. Flow temporarily continues through the central portion of the patch until the mesh becomes closed over with fibrin and, later, endothelial tissue. Thus, a gradual closure of the defect is effected. This is similar to Lillehei's perforated-compressed-polyvinyl-sponge technique. It is simpler than creating a temporary artificial ductus.[5]

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*Available from Mr. Norman C Jeckel United States Catheter and Instrument Corp., Glens Falls, N Y

2. *Smaller defects around 1 cm. in diameter with strong fibrous rims:* For these cases, the Mersilene sutures are placed in the tissue in the same way as for the large defects. However, the needles are passed tangentially through each side of a cigarette-shaped, noncompressed polyvinyl sponge ⅜ of an inch in diameter (see Fig. 2). The sutures are placed near the edges of the sponge so that, when they are tied down, some of the sponge is wedged between the edges of the defect. Thus, good closure is achieved without producing excessive tension on the septal tissue (see Fig. 2). The excess polyvinyl sponge is cut away, leaving a small, compact tampon in and over the defect. This method is similar to that reported by Kirklin.[1]

DISCUSSION

Age Range.—The average age of the patients in this series was slightly under 6 years, with extremes of 3 months and 33 years. Cardiac by-pass was deliberately avoided in patients under 1 year of age because of the high mortality in this age group. Instead, a two-stage approach has been employed for those infants requiring surgery to prevent recurrent heart failure and repeated respiratory infections. The first stage consists of banding the main pulmonary artery with a Dacron cloth band* to reduce the left-to-right shunt. When the child is older and can well tolerate open-heart surgery, the constriction in the pulmonary artery and the septal defect are corrected.[6]

Size and Location of Defect.—The largest defects were approximately 25 mm. in greatest diameter. Twenty-eight were located in the posterior septum behind the septal leaflet of the tricuspid valve. Eighteen were located in the outflow tract below the medial limb of the crista supraventricularis. Three were found immediately beneath the pulmonary valve. In only four of those located in the posterior septum was it necessary to transect (and resuture) a papillary muscle in order to gain good access to the area. This was done early in our series, but with increased experience and the adoption of small atraumatic needles, it is no longer used. In 4 patients, there were multiple ventricular septal defects: 3 had two, and 1 had eight, separate defects.

Associated Defects.—Three patients in our series had a patent ductus arteriosus. Two of these were closed at the same time. In one child, with equal pulmonary and aortic pressures, the ductus was temporarily occluded during the cardiopulmonary bypass while the ventricular septal defect was being closed, but afterward was allowed to remain open. This was done as part of a two-stage approach to the problem of severe pulmonary hypertension. The ductus was successfully closed at an operation undertaken 6 months later.[5]

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*Seamless tubing ("Helanca Dacron warp"), 8 mm. width. Available from John Sidebotham, Inc., 4317 Griscom Street, Frankford, Philadelphia 24, Pa.

Four patients had atrial septal defects of the secundum type, varying from about 5 mm. to 15 mm. in diameter. The presence of this defect was suspected by the appearance of bright red bronchial blood passing up through the tricuspid valve after the ventricular defect had been closed. The secundum area was then visualized through the tricuspid valve. The defect was then repaired with a continuous double row of 3-0 atraumatic Mersilene suture through a suitable atrial incision.

In two instances a pulmonic valvular stenosis was also present. Cardiac catheterization demonstrated a pressure drop across the valve, but the stenosis was of such a moderate degree that a large left-to-right shunt persisted. These cases were classified as interventricular septal defects with pulmonic stenosis rather than as acyanotic examples of tetralogy of Fallot. No cases of an infundibular stenosis are included in this series.

Two patients were discovered to have aortic insufficiency following closure of their interventricular septal defects. In 1 case, the septal defect was very large (25 mm.) and was associated with a large left-to-right shunt. Because the aorta was very small one wonders whether there was actually a leaflet defect present or whether the appearance of valvular incompetency was due to dilatation of the aortic ring from the increased systemic flow. The other patient's defect was located above the medial limb of the crista supraventricularis just below the pulmonic valve. Her insufficiency is the most severe of the two. This, together with the location of the septal defect, suggests that there is probably an associated defect in one of the aortic leaflets.

There was 1 patient who had congenital mitral insufficiency and 3 with tricuspid insufficiency. The child with mitral insufficiency had pronounced clubbing and deficiency of the posterior leaflet of the mitral valve. She also had severe vascular changes in the small muscular arteries. The 3 patients with tricuspid insufficiency had, in effect, a left ventriculo-right atrial shunt. This resulted from a cleavage of the septal leaflet of the tricuspid valve. In each instance, the valve leaflet was repaired along with the septal defect.

Persistent Shunts.—There are 2 patients in whom sizable left-to-right shunts persist. These should be regarded as operative failures and will require re-operation. One of these was a 1 cm. defect closed only with interrupted atraumatic silk sutures. In the other, a large defect, a double thickness patch of Teflon cloth was sewn in place employing a mattress suture technique as described earlier. It is believed that in the first patient, the suture line disrupted (at least partially) after cardiac contraction had resumed. The second failure may have been due to the inability of the Teflon cloth to apply itself snugly to the septum. Both of these patients were early cases who underwent operation before the present technique was evolved.

In 3 patients, there is a residual Grade 1-2 systolic murmur over the pulmonic area. They may be due to turbulence in the outflow tract (from dilatation of the pulmonary artery) from a residual leak in the repair, or possibly, from an overlooked second very small defect. In any event, the salutary clinical response and the return toward normal of the electrocardiogram, roentgenogram, and hilar activity suggest that these murmurs are physiologically inconsequential.

Mortality.—There were 9 deaths in this series. Seven had high pulmonary vascular resistance as evidenced by catheterization studies showing essentially systemic pressures in the pulmonary circulation and predominant right ventricular hypertrophy on the electrocardiogram. All but one occurred during the first 6 months of our open-heart program. Initially, these deaths were blamed on the vascular changes because they all seemed to die a respiratory death. Pulmonary edema and interalveolar hemorrhage were prominent at autopsy. In retrospect, many of the deaths probably should be attributed to the techniques in use at that time. The addition of serum albumin* to the perfusate in sufficient quantities to balance osmotically the saline used in the donor bottles and in priming the pump has contributed importantly to the elimination of these pulmonary complications.[7] Tracheotomy is now rarely needed.

Two deaths occurred in the moderate hypertensive group. In both, the hypertension was due to large pulmonary flow. One was 18 months old and the other 3 months old. The former had a large ductus and an atrial septal defect. Pulmonary edema was found at autopsy. This is a preventable death. The 3-month-old infant now would not be submitted to cardiopulmonary bypass, but managed in two stages as described.

There was one death in the nonhypertensive group. This child, 24 months old, died unexpectedly 24 hours postoperatively following a tachycardia of 180. Presumably, this passed into ventricular fibrillation. No explanation could be found at autopsy.

CONCLUSIONS

Heart block complicating the surgical repair of interventricular septal defect is due to direct injury to the septal area bearing the conduction pathways. This injury may be produced during or following the improper placement of sutures or, perhaps, by pressure on the septum by a hard patch material. The presence of high pulmonary vascular resistance has not influenced the incidence of heart block or heart arrythmia.

In our series, the mortality is primarily related to the psysiologic consequences of a high resistance in the pulmonary vascular bed. In those cases in which the pulmonary hypertension is due to increased flow, no special measures for correction of the defect are required. However, in patients with advanced changes in the small muscular pulmonary arteries and minimal left-to-right shunt, a gradual closure is helpful in improving immediate postoperative survival. The ultimate course of these patients will depend upon the degree of restitutions that will take place in the media and, particularly, in the intima. Following repair, the situation becomes similar to the pathologic physiology of the patient with severe pulmonary vascular changes secondary to long standing mitral stenosis Persistence of a high pressure in the pulmonary arterial bed may further aggravate the changes in these vessels so that regression cannot occur

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*Kindly supplied by Dr. Paul W. Yost, The American Red Cross Blood Program.

SUMMARY

A surgical technique is presented which has successfully avoided the complication of heart block in all cases of interventricular septal defect This injury can be produced by the improper placement of sutures or, we believe, by pressure from a hard patch material Therefore, it is important to avoid incorporating the conduction pathways in the sutures and to prevent crushing the conduction area against hard patch material This method of placing the sutures avoids encircling the fibers and the two component patch eliminates the need for excessive pressure by the patch against the septum The patch can be modified to effect a gradual closure in patients with high pulmonary vascular resistance

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CONGENITAL DIAPHRAGMATIC HERNIA IN THE ADULT

A New Technique in the Closure of the Bochdalek Hernia

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HERNIATION through the space of Bochdalek is the most common type of congenital diaphragmatic hernia. This defect is usually seen in infancy but, while occurring much less frequently in the adult, it remains a clinically significant group. Bowditch,[1] in 1853, analyzed 88 patients with diaphragmatic hernias and found that 9 of the 22 with the congenital type lived after the second year of life without surgical intervention. This would suggest that a small number of these patients surviving the high mortality during the first year of life may live to a significant older age. Liebow[2] cites 9 cases of massive congenital diaphragmatic hernias in which the patients lived to the ages of 17 to 50 and suggests that long life is not incompatible with this condition. This report is concerned with the recognition and treatment of the Bochdalek hernia in the adult.

The diaphragm is a complex organ made up of two major components embryologically, which shift their position during fetal life under different time schedules of development. The upper or ventral portion of the diaphragm is formed by the septum transversum which develops in the cervical region of the paired third and fourth myotomes and migrates caudad to the first lumbar segment in the 2-month embryo. The transverse septum then fuses with the ventral mesentery. The dorsal portion of the diaphragm develops from the paired pleuroperitoneal membrane which is derived from the pulmonary ridge. Medially, the membrane fuses with the dorsal mesentery to form the posterior and central portion of the diaphragm and contains the esophageal hiatus. Mesodermal cells derived from the receding wolffian bodies fuse to form the right and left crura of the diaphragm. The pleuroperitoneal canal is closed by concentric growth of the membrane at the end of the seventh week of fetal life and complete development of the diaphragm is accomplished by fusion of this membrane with the septum transversum and derivatives from the lateral chest wall (Fig. 1). Arey[3] believes that the closure of the pleuroperitoneal communication is not due to active growth of the membrane but rather by passive expansion caused by growth of adjacent lungs, liver, and adrenals. The Bochdalek hernia results from incomplete closure of the pleuroperitoneal canal. In

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the tenth week of fetal life viscera return from the umbilical cord to the abdominal cavity and, if the canal is open, loops of bowel will herniate into the pleural cavity The small bowel having greater mobility and lesser bulk enters the pleural space first, followed by the splenic colon Stomach is the last to herniate, rotating 180 degrees so that its fundus lies cephalad The Bochdalek hernia contains no peritoneal sac and is therefore a false hernia A true hernia developing as a result of weakness of the fused pleuroperitoneal membrane is a rare condition

Paul and Kanagasuntheram[1] find a definite sequence of bowel herniation in all Bochdalek hernias From an analysis of two autopsies and a study of all other existing reports they find that the hernia is due to incomplete closure of the pleuroperitoneal canal with orderly sequential herniation of small bowel, followed by splenic colon and stomach They observe that no Bochdalek hernia has ever been reported with only stomach present in the left chest The Bochdalek space is between the twelfth rib and the septum transversum and not between the twelfth rib and the vertebrae as Keith states (Fig 1) When the left diaphragmatic crura, as well as the pleuroperitoneal membrane, is underdeveloped, the hiatus will extend from the vertebrae to the septum transversum Herniation of the kidney and adrenal may then be present It is apparent that repair of this defect will be somewhat different from that of the typical Bochdalek hernia

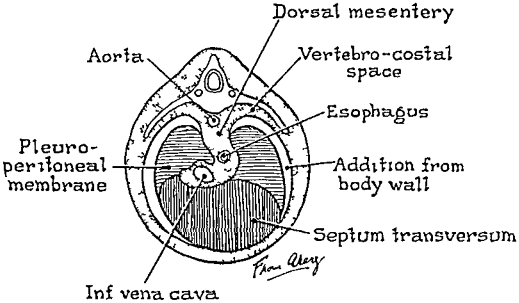

Fig 1 —Anlagen of the diaphragm Note that Bochdalek space is contained between twelfth rib and septum transversum

The pleuroperitoneal hernia may be small and localized close to the ventral septum or encompass the entire posterolateral portion of the diaphragm The most common anomalies associated with this type of hernia are incomplete rotation of bowel and incomplete development of the left lung

CASE REPORT

B H, a 56 year old white woman, was first seen on Oct 31, 1955, complaining of marked dyspnea, fatigue and pains in the left chest, back, and neck For a number of years, she had had epigastric and left upper quadrant pain associated with marked eructation, nausea, and vomiting. Nine years before, an abdominal laparotomy had been performed at another hospital. Repair of a left diaphragmatic hernia was said to have been attempted through a 6-inch incision over the left tenth rib, but no operative report was recorded. Since this operation, she has noted increased dyspnea on exertion, but her digestive symptoms have remained unimproved. In 1952, x-ray studies of the stomach revealed displacement of the stomach and small and large bowel into the left hemithorax. The patient has always been somewhat fatigued and short of breath.

On physical examination she did not appear to be acutely ill and exhibited no respiratory difficulties at rest. The right lung was clear to percussion and auscultation, and the right diaphragm moved well. The percussion note over the left hemithorax was tympanitic, no breath sounds but active peristaltic sounds were heard. No retrocardiac dullness could be delineated. There was a well-healed 6-inch scar over the left tenth rib. The abdomen was soft with no masses, but increased peristaltic activity was noted.

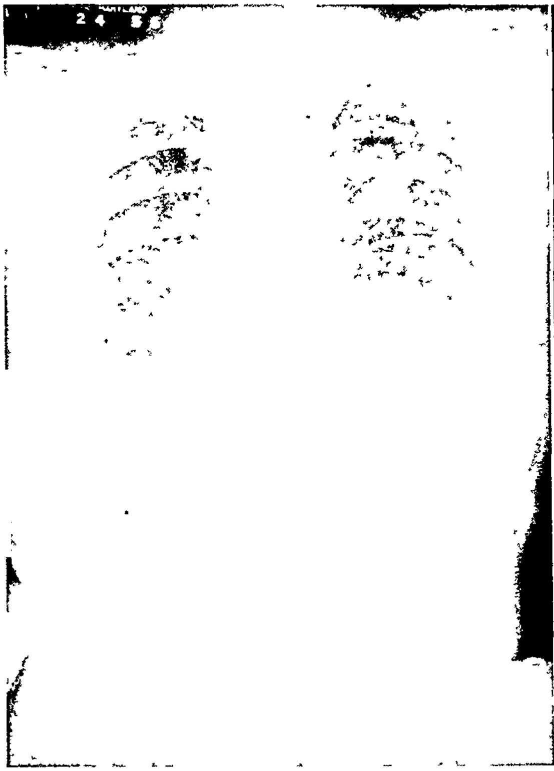

Fig. 2.

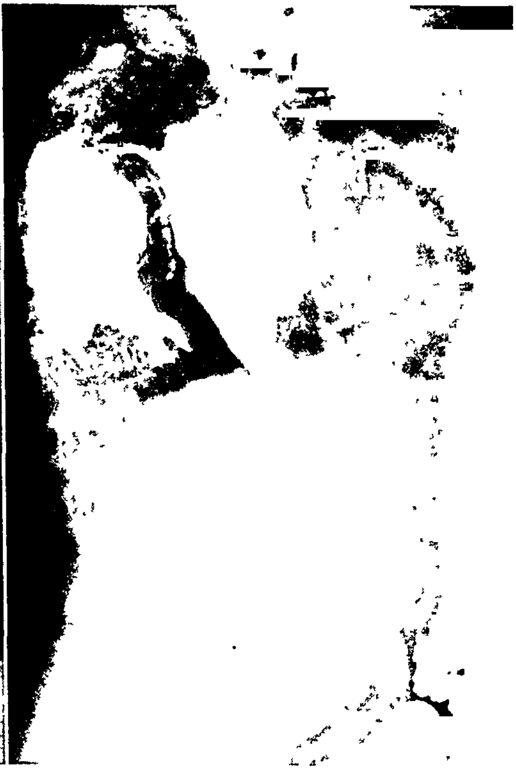

Fig 3

Fig. 2.—Chest film following pneumoperitoneum showing left pneumothorax, dilated stomach, barium streaks in large bowel, scalloped border of colon, compressed left lung, and mediastinal shift

Fig. 3.—Gastrointestinal series reveals stomach rotated 180 degrees within left pleural space with small bowel anteriorly placed and colon filled with air at apex

Roentgenographic examination of the chest revealed the heart and mediastinum to be shifted toward the right due to the presence of colon, small bowel, and stomach in the left hemithorax (Fig. 2). There were multiple linear strands of atelectasis at the left apex. The right lung appeared normal. Barium studies revealed rotation of the stomach through 180 degrees with the fundus placed cephalad at the level of the third rib (Fig. 3). The splenic flexure was herniated into the left hemithorax, rising to the apex of the chest (Fig. 4). Following pneumoperitoneum, air was noted at the apex of the left chest with both colon and stomach displaced downward.

The patient was admitted to Sinai Hospital on Jan. 22, 1956, for repair of a left Bochdalek diaphragmatic hernia. Through a left thoracotomy approach, a large posterolateral defect of the left diaphragm was found (Fig. 5). The anterior or ventral portion of the diaphragm was thick and contracted. A small, thick ridge of tissue was present along the twelfth rib. The esophageal hiatus was normal and the left crura was evident. There were no adhesions binding the stomach, or small and large bowel to the pleural wall and reduction was accomplished without difficulty. The apical, posterior and anterior segments of the left upper lobe appeared normal, contained carbon pigment, and expanded freely, but the entire left lower lobe and the lingula of the left upper lobe were flesh pink, without pigmentation and large blebs were seen along the periphery of these segments. Repair of the outer half of the diaphragmatic defect was accomplished by approximating the thick ventral leaf to the short muscular ridge and periosteum overlying the twelfth rib. A large defect, measuring 6 cm. in diameter, was still present following this partial repair (Fig. 5, *A*). Sutures placed through the muscular edges close to the esophageal hiatus tore out with each strong pulsatile thrust of the heart. In an attempt to free the diaphragm from this abnormal motion, the anterior, left lateral, and posterior attachments of the pericardium to the diaphragm were freed, and it was then possible to suture together the remaining edges of the defect (Fig. 5, *C*). Numerous blebs in the lower lobe were clamped and their base sutured. The left lung was easily inflated and filled the entire left hemithorax. The postoperative course of the patient was marked by repeated spontaneous pneumothoraces, apparently due to recurrent bleb ruptures, and this complication necessitated several aspirations and tube drainage. On discharge, 2 weeks after the operation, she felt well and had no digestive symptoms or dyspnea. On her last visit in January, 1959, she felt well, had no digestive symptoms, and stated that for the first time in her life she was able to shop without fatigue or dyspnea. Her left lung was well expanded (Figs. 6 and 7) and there was definite, though slight, impairment of motion of the left diaphragm.

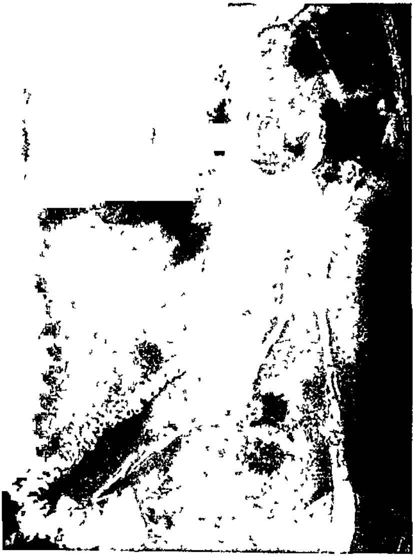

Fig. 1—Barium enema study showing malplacement of colon in left chest

DISCUSSION

Symptoms.—Cardiorespiratory and digestive symptoms associated with the Bochdalek hernia are due to the compression and distortion of the herniated bowel as well as lung and mediastinal structures. Volvulus with obstruction and perforation may occur within the hemithorax and present abdominal symptoms but without localizing signs of peritoneal irritation. In the present case, the patient had ventilated her right lung together with a small portion of the left upper lobe. The bleb formation, absence of pigmentation, and recurrent pneumothorax suggest maldevelopment and congenital atelectasis of the lingula and left lower lobe. Recurrent incomplete volvulus of the bowel gave rise to the abdominal pain, nausea, and vomiting.

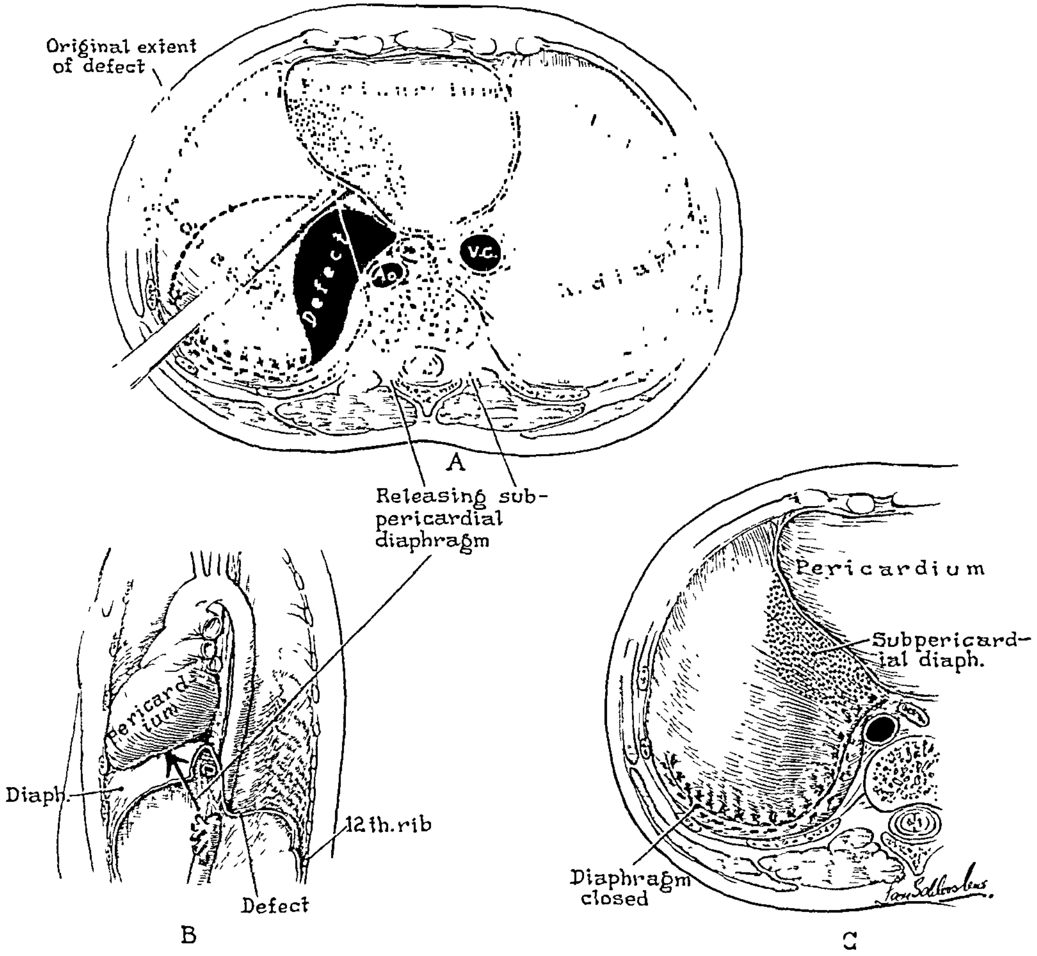

Fig. 5.—*A*, Appearance of large Bochdalek hernia after reduction of bowel. Note posterior muscular ridge and pericardial attachments. *B* and *C* show method of repair utilizing posterior muscular ridge and ventral portion of diaphragm after pericardial attachments are released.

Diagnosis.—Inspection of the chest will reveal decreased expansion of the affected side. The percussion note may be either dull or tympanitic depending upon whether the herniated bowel contains predominantly air or fluid. The heart is displaced to the right and no retrocardiac dullness is noted. When intestinal sounds are heard within the chest, the correct diagnosis is evident. In the presence of a typical history of intestinal obstruction, a flat, nontender abdomen should suggest the possibility of a diaphragmatic hernia

Roentgenographic examination of the chest shows displacement of the heart and mediastinum to the right. Fluid levels will usually be seen which might be incorrectly interpreted as encapsulated hydropneumothorax. Lateral x-ray films and barium studies will usually reveal the stomach to be lateral to the pericardium and the splenic flexure at the apex of the chest Pneumoperitoneum will reveal the absence of a hernial sac

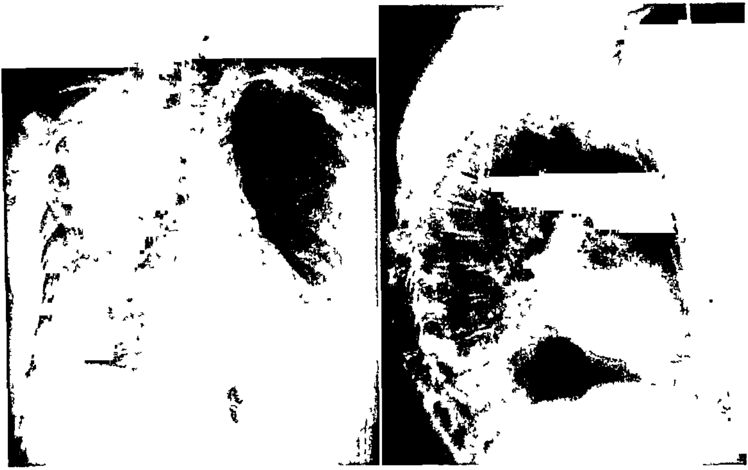

Fig 6 Fig 7

Figs 6 and 7—Chest films made 2½ years after operation showing well-expanded left lung with bowel below diaphragm

Treatment.—Repair of the Bochdalek hernia in the adult is usually an elective procedure although the presence of such complications as intestinal obstruction or perforation makes immediate correction necessary. In all cases, the transthoracic approach should be used The bowel should be decompressed prior to operation In the absence of previous infection, no adhesions are noted binding the bowel to the chest wall and reduction of the bowel into the abdomen is a simple procedure.

Numerous methods have been used in the repair of the Bochdalek hernia.[9, 10, 11] Thoracoplasty has been utilized in order to decrease this space and allow dorsoventral approximation, but ventilation of the lung is thereby lost. The latissimus dorsi muscle has been used[7] to close the lateral defect of the diaphragm and this is probably of little value since muscle atrophy will take place as the muscle moves across the exposed rib Rives and Baker[8] have suggested the approximation of the transversalis fascia to the dorsal edge of the diaphragm, but it is difficult to see how sufficient fascia would be available to accomplish this. Free fascia or fascia lata has been used but may be expected to exhibit paradoxical motion, may eventrate, and even atrophy. Adler and Firmie[12] have studied plastic materials and found nylon net or mesh to be tough, durable, inert, and somewhat pliable. This material can be used only as the partitioning membrane and obviously will not take part in the diaphragmatic motion. Tantulum mesh has been used but is known to fragment in time. Steel mesh may not fragment but is too rigid and may bring injury to contiguous bowel or blood vessels.

In small and medium defects of the pleuroperitoneal membrane, closure may be accomplished by the use of coapting sutures of nonabsorbable suture material. If there is marked diaphragmatic activity, injection of procaine (1 per cent) about the phrenic nerve has been suggested to produce temporary paralysis, but is unnecessary when the anesthesiologist can control its movement. In the large circular defects having a complete circle of muscular tissue, the repair of the lateral edge may be accomplished by sutures opposing the ventral muscular ridge with the tissue about the twelfth rib. The paraesophageal area, however, may be impossible to close and it is this type of defect in which repair can be accomplished by freeing the pericardial attachments to the diaphragm. Release of the anterior, left lateral, and posterior attachment of the pericardium allows the ventral or septum transversum portion of the diaphragm to be brought down and sutured to the posterior costal portion of the diaphragm. The release of the pericardium removes the continued motion of the heart on the suture line (Fig. 5). The case cited accomplished this type of repair.

When there is absence of the pleuroperitoneal membrane, as well as loss of a vertebrocostal margin, no posterior muscular ridge is present. This defect may be associated with the presence of a high kidney or adrenal herniating into the hemithorax. Prosthetic materials such as steel mesh, Dacron, or Orlon sheeting have been suggested but are either too rigid or exhibit paradoxical motion with respiration. Repair of this defect may be accomplished by elevating the remaining ventral portion of the diaphragm and suturing it to the preformed intercosto-periosteal muscle flap which may be developed from the posterolateral aspect of the fifth and sixth ribs. We have experimentally produced this defect and accomplished this type of repair in dogs,[6] with subsequent return of normal diaphragmatic motion.

SUMMARY

Congenital diaphragmatic hernias of the Bochdalek type are rare in adults but are found in a clinically significant group of patients. Diagnosis usually depends upon symptoms arising from distortion of bowel, compression of the left lung, displacement of the heart and mediastinum, and x-ray evidence of bowel herniation. Repair of the large hernias have not been gratifying in the past due to the lack of approximating muscular tissue. In very large posterolateral Bochdalek hernias, without a rim of posterior muscular tissue, elevation

of the diaphragm with suture of the ventral septal tissue to a periosteo intercostal muscle flap at a higher rib level is suggested When large medial defects are present, the removal of pericardial attachment to the diaphragm will allow secure closure A successful case of this type is reported

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Congenital diaphragmatic hernias of the Bochdalek type are rare in adults but are found in a clinically significant group of patients. Diagnosis usually depends upon symptoms arising from distortion of bowel, compression of the left lung, displacement of the heart and mediastinum, and x-ray evidence of bowel herniation. Repair of the large hernias have not been gratifying in the past due to the lack of approximating muscular tissue. In very large posterolateral Bochdalek hernias, without a rim of posterior muscular tissue, elevation

In 1946, Holt[5] reviewed the problems of esophageal atresia and tracheoesophageal fistulas and suggested that a fourth type be added to Vogt's classification, namely: esophagorespiratory fistula without atresia of the esophagus. While this is an uncommon malady in infants, it is rarer still in adults, with only 13 documented cases reported in the literature to date.[6-13]

The major clinical and physical findings have been related to the inevitable pulmonary sepsis which develops with this lesion. Most patients have histories of repeated bouts of pneumonia and cough, often producing purulent sputum. Food particles may be raised with the sputum and hemoptysis is a common complaint. Whether or not this is secondary to the commonly found bronchiectasis, or merely a manifestation of the severe chronic bronchitis, is open to speculation. The relative rarity of this lesion has prompted the present report of congenital esophagorespiratory fistulas in 2 adult patients in whom the diagnosis was proved by surgery or postmortem examination.

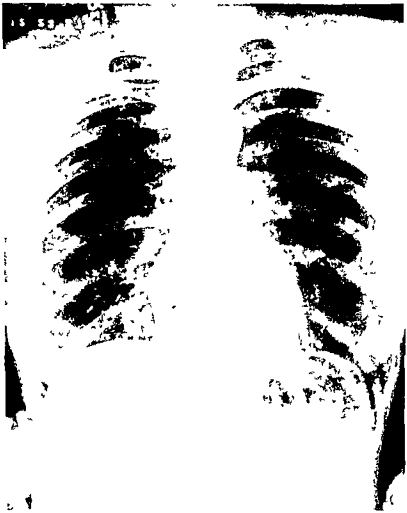


Fig 1.—Chest roentgenogram (Case 1) which shows chronic peribronchial infiltration but no evidence of consolidation or pneumonitis The patient had had repeated bouts of pneumonia and dyspnea.

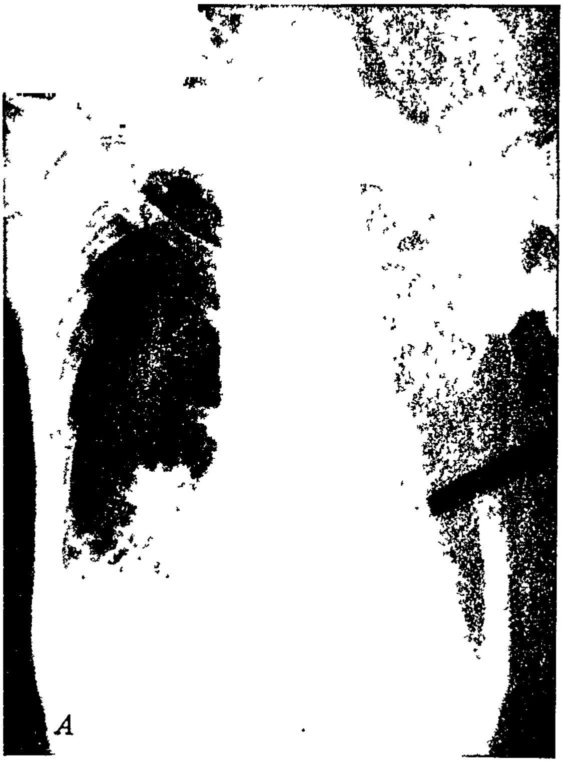
CASE REPORTS

CASE 1.—M. W., a 63-year-old white woman, was admitted to the thoracic surgical service of Akron City Hospital on Dec. 22, 1957, with chief complaints of chronic malaise, cough, and recurrent pneumonia (Fig. 1). The patient stated that she had been short of breath as long as she could remember and that she had been a "blue baby" at birth. She had frequent bouts of wheezing and cyanosis as a child and was treated on innumerable occasions for pneumonia. "Choking spells" were related to the ingestion of food and liquids but there had been no hemoptysis and no food particles were ever raised. Copious quantities of whitish sputum were raised with postural drainage. In 1941, following a complete examination including bronchoscopy and esophagoscopy, a diagnosis of high-lying tracheoesophageal fistula was made. Surgical treatment was considered but turned down because of the apparent high risk.

The past medical history was notable only in that it included diphtheria at an early age, and hysterectomy with appendectomy at age 33. The family history was noncontributory.

Positive physical findings were limited to the chest where fine crepitant râles were heard posteriorly. There was considerable wheezing with respiration but no dyspnea was present. The vital signs were normal.

Laboratory studies revealed a chronic urinary tract infection. The fasting blood sugar, blood urea nitrogen, and hematologic studies were within normal limits.

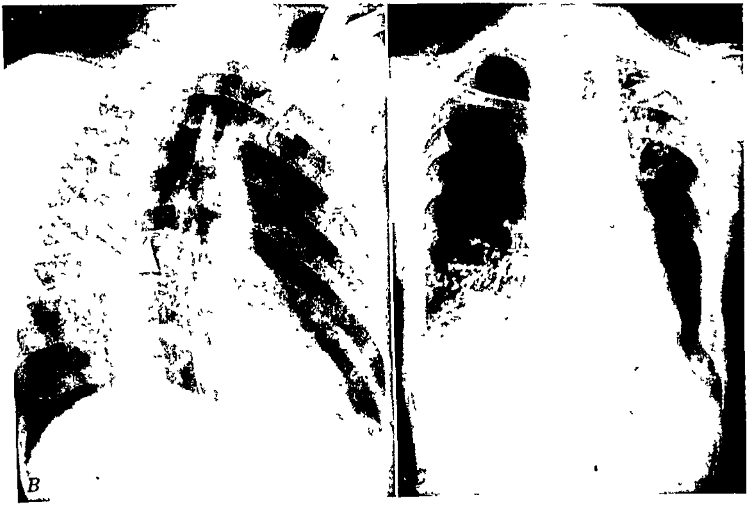


A.

Fig. 2.—*A*, Roentgenogram of the chest (Case 2) which shows chronic and acute pneumonic process involving the right middle and lower lobes.

At esophagoscopy and bronchoscopy on Dec. 24, 1957, under local anesthesia, no fistulous tract could be identified. On December 27, the patient was given a swallow of iodized oil but again the fistula could not be demonstrated. Only a moderate irregularity of the esophageal mucosa was noted at the sternal notch. On Dec. 30, 1957, bronchoscopy and esophagoscopy were repeated and a small, high-lying, tracheoesophageal fistula was found at the level of the suprasternal notch. A curved director was passed through the fistula and was visualized in the esophagus. On Jan. 6, 1958, under endotracheal anesthesia, the patient was operated upon by one of us (W. F.) for closure of the defect. A low collar incision was made through the skin and platysma muscle and the strap muscles were separated. The right sternocleidomastoid muscle was retracted laterally and the right inferior thyroid artery was divided at its origin. The right lobe of the thyroid gland was mobilized and retracted medially along with the right recurrent laryngeal nerve. The trachea was freed by blunt dissection and a small tracheoesophageal fistula was exposed. It lay at the level of the fourth cartilaginous ring and was quite short, measuring 1 cm. in length by perhaps 7 mm. in transverse diameter. Since the lesion was extremely short, it was decided to ligate the fistula in continuity. By utilizing the sterile bronchoscope, a soft esophageal dilator was threaded through the fistula as a guide and two 2-0 silk suture ligatures were placed around the fistula. These were tied down after removal of the guide. The wound was closed anatomically and it healed without incident. The patient improved symptomatically and has remained well to date.

Case 2.—C. J., a 60-year old white man, was admitted to Akron City Hospital with complaints of bloody diarrhea alternating with constipation of several months' duration. He subsequently was found to have carcinoma of the rectum and underwent a combined abdominal-perineal resection. During the fluoroscopy accompanying an upper gastrointestinal x-ray study prior to surgery, a large bronchoesophageal fistula was noted which connected the esophagus with the right main-stem bronchus (Fig. 2, *A*, *B*, and *C*). Closer questioning of the patient at this time revealed a history of pulmonary sepsis for over 40 years. He stated that he had been chronically ill as a child and had repeated bouts of pneumonia coupled with chronic cough and fever. There was a past history of diphtheria at the age of 8 years. He was told by a physician, at that time, that he had "ulcers on his bronchial tubes." He stated that he would "almost strangle" with pharyngeal secretions at night, and that these symptoms were worse when lying on his right side. The patient had been treated on eight occasions for pneumonia and had had three or four extensive pulmonary hemorrhages. He had been jaundiced in 1945 and had been treated for chronic gall bladder disease since that time.



B

C.

Fig 2. Cont'd—*B*, Oblique view of the chest (Case 2) which shows passage of radiopaque medium from the esophagus into the large bronchoesophageal fistula to the right main-stem bronchus

C, Roentgenogram (Case 2) after ingestion of radiopaque medium The bronchogram thus produced showed massive bronchiectasis and chronic pulmonary suppuration of the right lower and middle lobes.

Because of the x-ray findings, bronchoscopy and esophagoscopy were performed under local anesthesia. The fistula was readily seen during both examinations. The mucosa of the tract, as well as that surrounding it, seemed grossly normal. The tract arose from the anterolateral aspect of the esophagus and communicated with the right main-stem bronchus near an accessory bronchus to the right upper lobe.

The patient was discharged and ultimately readmitted with terminal carcinomatosis. The autopsy revealed massive metastatic carcinoma in the liver and abdominal lymph nodes. The previously described fistula was seen to connect the esophagus and the right main-stem bronchus (Fig. 3). The tract was well defined and appeared to be of congenital origin. There was accompanying long-standing right lower lobar pulmonary suppuration with abscess, bronchiectasis, and pulmonary fibrosis.

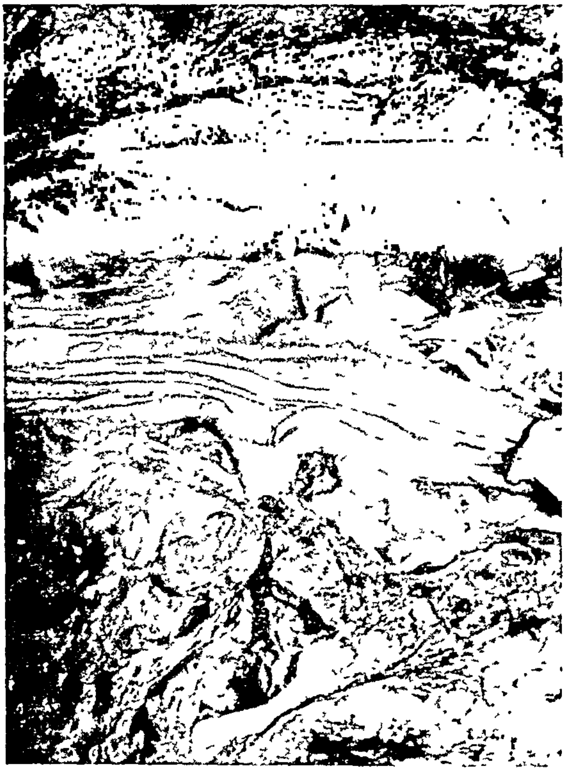


Fig. 3.—Photograph of the autopsy specimen in Case 2. The large bronchoesophageal fistula is seen extending into a large area of necrotic pulmonary parenchyma.

SUMMARY

Congenital esophagorespiratory fistula in the adult is a very rare anomaly with only 13 documented cases having been published to date. The disorder is accompanied by severe long-standing pulmonary sepsis and is usually diagnosed by careful history and often as an accidental finding. Two additional cases of fistulous connection of the esophagus and tracheobronchial tree in adult patients have been presented. Esophagorespiratory fistula without esophageal atresia may be compatible with long-term survival and may be difficult to diagnose without repeated radiologic and endoscopic examinations.

We wish to express our appreciation to Mr. John Muldowney, Akron City Hospital, for the photographs used in this paper.

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PULMONARY ALVEOLAR PROTEINOSIS

Review of the Literature and Report of a Case

Leldon P. Pitt, M.D., Philadelphia, Pa.*

In June, 1958, pulmonary alveolar proteinosis was first reported in the literature[1] and was given this title by the authors—Dr. Samuel Rosen, Chief of Pulmonary Pathology, Armed Forces Institute of Pathology, Dr. Benjamin Castleman, Clinical Professor of Pathology, Harvard Medical School, and Dr. Averill Liebow, Professor of Pathology at Yale University. The first case was actually seen by Dr. Castleman in July, 1953, the specimen having been obtained by lung biopsy which proved puzzling to him; whereupon he sent the slides to Dr. Liebow who likewise recalled never having seen such lesion. Since 1955, slides for consultation have been received by the above pathologists at an increasing rate so that by June, 1958, a total of 27 cases had been compiled. Some patients were studied in their respective institutions, but the majority were studied by slides sent from various states in this country and from three foreign countries—Turin, Italy; London, England; and Canada.

This perplexing disease is characterized clinically by an insidious onset of progressive dyspnea, cough which may not be productive but often is productive of white, yellow and, at times, blood-streaked sputum, frequent chest pains, fatigability, and later by weight loss, clubbing, and cyanosis. Temperature is normal or slightly elevated. Physical examinations in the cases studied were not remarkable except for the above signs.

The ages ranged from 2 years to 56 years, but the majority were between 20 and 50 years of age. The occupations listed were as follows: lumberyard employee,[4] carpenter, electrician exposed to smoke in the production of cannon shells, butcher, animal cage cleaner, painter, machinist, toothpaste factory worker, and welder (father of the child).

CLINICAL STUDIES

Laboratory Studies.—In general, the erythrocyte counts and hematocrits were normal or slightly elevated (hemoglobin, 15 to 18 grams). The leukocyte counts varied from normal to 20,000, probably depending upon the amount of superimposed infection. Sputa smears and cultures were generally negative for common pathogens and tubercle bacilli, as were the few lung specimens that were

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examined for fungus Attempts to isolate virus were unsuccessful In 2 cases there was superimposed fungus infections—one Cryptococcus and one Nocardia, both of which terminated fatally Skin tests for tuberculosis, histoplasmosis, blastomycosis, and brucellosis gave various reactions which were of no help in diagnosis Total serum proteins and A G ratios were generally normal as were cholesterol, total lipids, calcium, phosphorus potassium, chlorides, nonprotein nitrogen, and blood sugars

X ray Studies—Radiographs were quite similar in all cases, being characterized by bilateral, diffuse granular, feathery or slightly nodular infiltrations radiating from the hilum and, in general, were more extensive in the lower two thirds of lung fields There was a notable absence of hilar adenopathy and no calcification has been observed

Pathology—Grossly, the lungs were heavier, firmer, less spongy, and more friable than normal There were diffuse confluent grayish areas of infiltrations from which, in some specimens, oozed milky fluid on sectioning The weight of some lungs was remarkable—as high as 3 500 to 4 000 grams at autopsy Microscopically, the alveoli were either partially or completely filled with eosinophilic granular, PAS positive, proteinaceous material in which there were varying numbers of foamy mononuclear cells The interalveolar septi were remarkably well preserved and showed essentially no cellular infiltration and no proteinaceous material It is thought that most, if not all of this protein material is derived from the transformation of the large mononuclear cells which line alveoli, the so called "septal cells" Mediastinal and peribronchial lymph nodes examined showed only reactive hyperplasia and some erythrophagocytosis and were not significantly enlarged grossly

Spectroscopic examination revealed no evidence of heavy metals and examination for radioactivity revealed none

CASE REPORT

The patient, T K, age 50 (U H No 31683), was a white male, ex stevedore whose chief complaint was progressive dyspnea of one year's duration This was associated with a nonproductive cough, intermittent nonspecific chest pains and, a few months before death, by marked cyanosis and clubbing of his fingers He had been treated by his family doctor for heart disease without improvement There was no history of hemoptysis, previous pulmonary diseases, or peripheral edema On the day of admission he had had several drinks of alcohol, he collapsed into unconsciousness which precipitated his initial hospitalization on Aug 31, 1958

Past medical history revealed no cardiovascular, renal, or gastrointestinal diseases He denied allergy, tuberculosis, or other serious illnesses

Social history revealed that he smoked a package of cigarettes per day and drank alcoholic beverages in large amounts at times He had worked as a stevedore until a year before admission when he had retired because of dyspnea There was no history of exposure to toxic fumes and dust or the consumption of oily materials

Physical examination revealed a chronically ill, well developed but poorly nourished man who had moderate dyspnea, cyanosis, clubbing of fingers, and coarse rales bilaterally The temperature was 101° F respirations 32 pulse 130, and blood pressure 110/80 mm Hg The heart was thought to be slightly enlarged but there was no evidence of decompensation There was no lymphadenopathy and no enlargement of the abdominal viscera

Laboratory data included hemoglobin 14 grams, hematocrit 42 mm., leukocytes 20,000 on admission with 79 per cent segmented neutrocytes, 19 per cent lymphocytes, and 2 per cent monocytes. After antibiotics, the leukocytes numbered 7,000 with a normal differential count. Urinalysis was normal, serum bilirubin, calcium, alkaline phosphatase, potassium, and blood urea nitrogen were normal. The phenolsulfonphthalein test showed 8 per cent retention in 45 minutes (normal 0-5), serum total proteins 7.0 grams per cent, albumin 3.5, and globulin 3.5. The transaminase varied from 28 to 52 units (normal 20-40), sedimentation rate 38 mm. per hour (normal 0-10). Multiple sputum studies were negative for tubercle bacillus and fungus but did show nonhemolytic streptococcus and *Staphylococcus albus.*

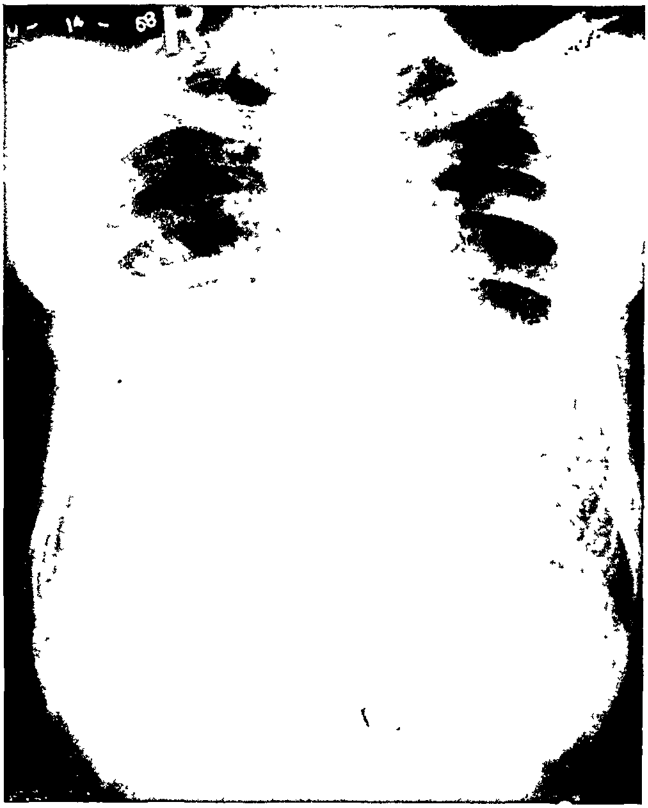

Fig. 1.—Film taken on Oct. 14, 1958, showed "soft cottony" infiltration chiefly in mid and lower lung fields.

Electrophoretic separation of serum proteins revealed hypoalbuminemia and hyperglobulinemia, the latter involving chiefly the alpha and beta fractions. The electrocardiogram showed changes consistent with subendocardial ischemia.

Skin tests for tuberculosis were positive on second strength, but were negative for histoplasmosis, blastomycosis, and coccidiomycosis.

Chest x-ray studies (Fig. 1) revealed bilateral, diffuse granular, or slightly nodular pulmonary infiltration most marked in the mid and lower lung fields and no hilar adenopathy. This was diagnosed as bronchopneumonia.

The administration of digitalis and tetracycline resulted in a return to normal temperature and symptomatic improvement, without radiographic changes in the chest. After leaving the hospital 3 weeks after admission, the patient was followed in the Out-Patient Department and was noted to have increasing dyspnea, cyanosis, weakness, and dizziness. He was readmitted on Dec. 17, 1958. A roentgenogram of the chest showed a progression of pulmonary infiltration. The following day, I performed a lung and pleura

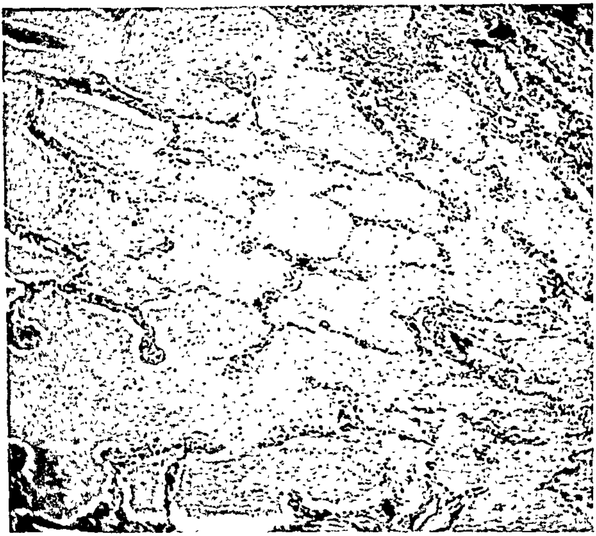

Fig. 2.—Hematoxylin and eosin preparation showing well-preserved, essentially normal alveolar septa and filling of alveoli with granular proteinaceous material. Note absence of inflammatory response.

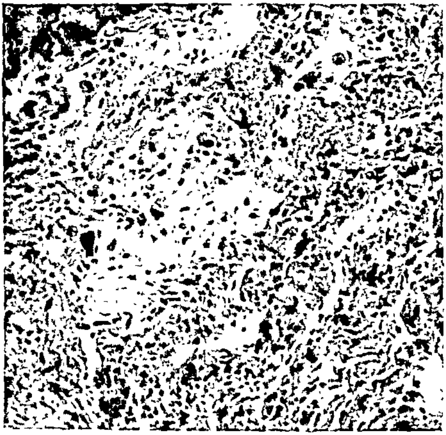

Fig. 3.—Note granular mononuclear septal cells and slit-like spaces which probably represent cholesterol crystals. Occasional multinucleated giant cells are also seen.

biopsy (Figs. 2 and 3) under 1 per cent procaine anesthesia, through the anterior right third interspace. There were fibrinous adhesions between the visceral and parietal pleurae; these surfaces were dull gray and three times normal thickness. The lung was soft and friable and, upon sectioning, a milky fluid oozed diffusely from the cut surfaces. The sutures cut through the lung parenchyma readily while closing the defect. After operation, his condition was unchanged and a roentgenogram showed no change in the chest. He again signed out 2 days after the operation. He was next seen on Jan. 8, 1959, when he was deeply cyanotic, dyspneic, and died soon after admission from respiratory insufficiency (Fig. 4).

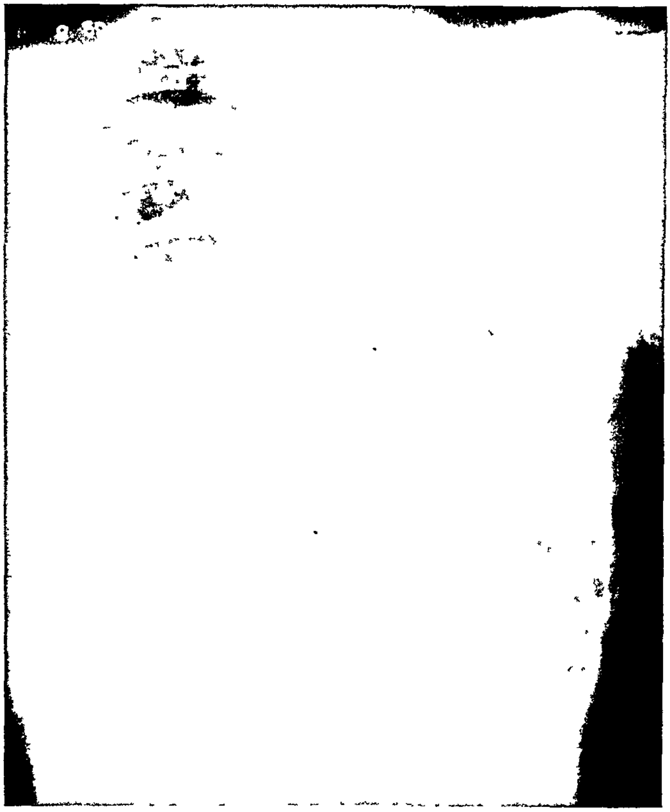

Fig. 4.—Film taken on the day of death, Jan. 8, 1959, showed extensive densities of both lungs

DISCUSSION

The etiology of this baffling disease remains unknown, but it is interesting to speculate in regard to the possible relationship to the inhalation of detergents, plastic fumes, and insecticides. Diseases most likely to be confused with this lesion are pulmonary edema, pneumocystis pneumonitis, and chronic interstitial pneumonia. Pulmonary edema presents a more acute picture which should respond to cardiorenal therapy. Pneumocystis infection usually occurs in premature infants who die in the second or third month of life. The roentgenogram may be quite like one of a case of proteinosis but examination of lung tissue reveals the parasites which produce this disease. Interstitial pulmonary fibrosis may be confusing clinically, but pathologically the picture is quite distinct from proteinosis. Miliary tuberculosis, sarcoidosis, and microlithiasis should offer little difficulty in differential diagnosis.

Therapy.—There is no known specific therapy as yet. Antibiotic and antifungus drugs are useful for superimposed infections but have no effect on the disease itself. Cortisone may produce temporary symptomatic improvement but has no lasting effect.

Prognosis.—Insufficient time has elapsed to gain significant data in this regard. In any case, however, prognosis should be guarded. Of the series reported, 5 patients were definitely improved at the time of report. One seemed to have fully recovered, both clinically and radiographically. In some, the symptoms improved but roentgenographic studies did not, and vice versa. Eight have died from pulmonary insufficiency. One patient died 4 months after onset, while another expired 4 years after onset of symptoms. Several patients have had negative x-ray studies of the chest from 3 months to 10 years before onset of symptoms.

Summary.—It seems unlikely that pulmonary alveolar proteinosis has been present for many years, as the pathologic characteristics are distinct and should not have been confused with previously known diseases. The onset is usually insidious and the clinical picture is characterized by progressive dyspnea, cough, often productive, and, later, cyanosis and clubbing of fingers. Radiographically, there is bilateral diffuse infiltration radiating from the hilum. Pathologically, the alveoli are filled with granular acidophilic protein material which is rich in lipids. The etiology and treatment are obscure and prognosis is uncertain. The only way to make a definite diagnosis in the living patient is by lung biopsy which can be done readily through a small intercostal incision under local anesthesia. I suggest this procedure be used more frequently for undiagnosed chronic pulmonary lesions.

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AORTIC-ESOPHAGEAL FISTULA

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Aortic-esophageal fistula occurs so infrequently that rarely does a surgeon see more than one case in a lifetime. Therefore it is not surprising that the diagnosis has been made usually at postmortem examination. This case is the only one that has been seen on two large thoracic surgical services in New York in 25 years. Although it presented the characteristics previously described in the literature, like so many others, the correct diagnosis was established after death.

CASE REPORT

O. M., a 4-year-old mentally retarded Negro girl, was admitted to the Thoracic Surgical Service of Triboro Hospital on July 21, 1958. Her chief complaints were only mild retrosternal pain which had been quite severe at its onset 3 days before admission, and dysphagia which had progressed, on admission, to the complete refusal of oral intake. A history of foreign body ingestion was denied by the patient and her parents. She appeared chronically ill with a temperature of 101° F., a pulse of 100, and a blood pressure of 120/80 mm. Hg. Her weight of 22 pounds was 15 pounds below normal. Dehydration was marked. The most prominent objective finding was substernal pain elicited by manual pressure. Examination of the heart and lungs was unremarkable. She had a hemoglobin of 14.3 grams, a hematocrit of 41.5 per cent, and a white count of 16,000. An emergency chest plate showed a foreign body, a coiled spring, in the esophagus, a right aortic arch, and minimal widening of the superior mediastinum (Fig. 1).

With a diagnosis of perforation of the esophagus and mediastinitis, thoracotomy was performed. Under general anesthesia using endotracheal technique, the right posterior mediastinum was opened extrapleurally through a paravertebral incision. Exploration revealed a right-sided aorta and the spring within the esophagus just below the arch. Its lower end had penetrated both the esophageal and aortic walls. All tissues were edematous but frank pus was not found. The esophagus was mobilized anteriorly and the sharp end withdrawn from the aortic wall and then by rotation it was removed from the esophagus. Neither bleeding nor leakage occurred after this maneuver, and therefore no attempt was made to close the minute perforations. The incision was closed with drainage of the posterior mediastinum. The foreign body was a spiral wire spring of two and one half turns with the diameter of a 20 gauge needle (Fig. 2).

The patient did well in the early postoperative period. After 3 days of parenteral feeding, oral intake was started and increased to a semisolid diet by the seventh day. The drains were removed on the seventh day. On the eighth day, after several tarry stools, the hemoglobin was 7.4 grams with a hematocrit of 26 per cent and normal bleeding and clotting times. Studies of the gastrointestinal tract revealed only some degree of malrotation. On

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the tenth postoperative day, mild shock with hypotension and tachycardia was attributed to gastric hemorrhage after fresh and dark clotted blood was aspirated from the stomach. A suspicion of blood dyscrasia was not substantiated by further detailed study. The situation was controlled on each occasion by blood transfusions. She improved until the thirteenth postoperative day when, following several black stools, she again showed hemorrhagic shock.

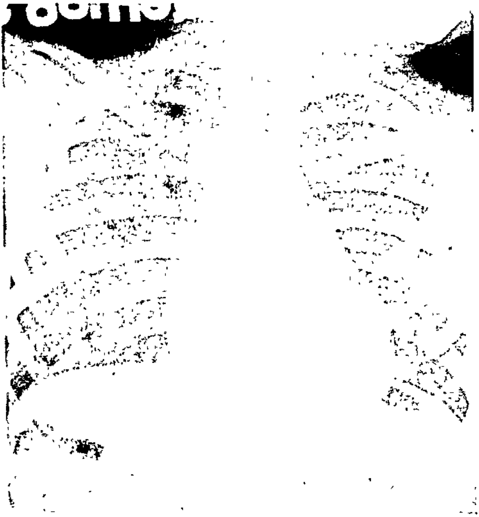

Fig. 1.—Roentgenogram showing the wire spring which perforated the esophagus and the right aortic arch.

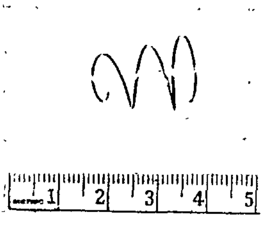

Fig. 2.—Photograph of the spiral spring.

A gastric tube was passed with particular attention to aspiration of the esophagus which did not yield blood. She again responded to transfusions. On the morning of the fourteenth postoperative day, she appeared alert and comfortable with a rapid pulse but she was not in shock. While a blood transfusion was being started she suddenly had a massive hematemesis and died.

At autopsy, a fistula between the esophagus and the arch of the right-sided aorta was demonstrated. This tract was 2 mm. in diameter and 1 cm. in length (Fig. 3). The tissue

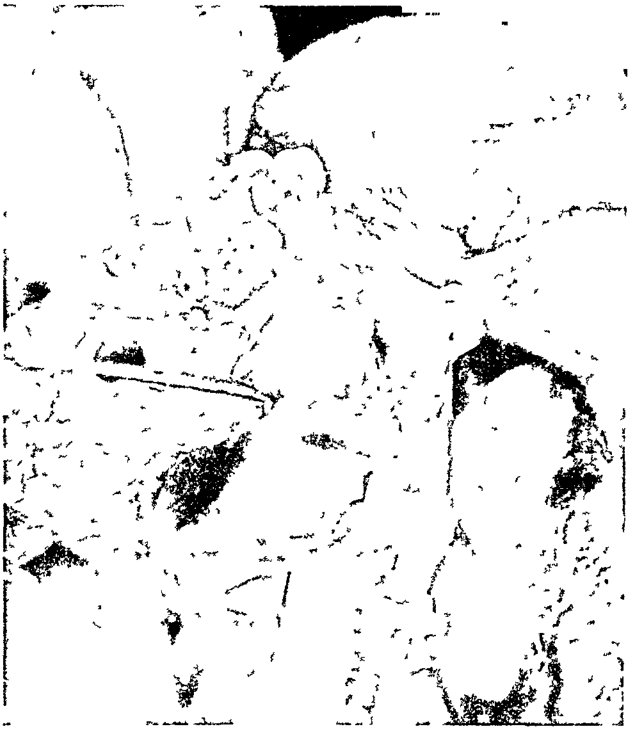

Fig 3 —Photograph of the opened esophagus with a probe in the fistulous tract.

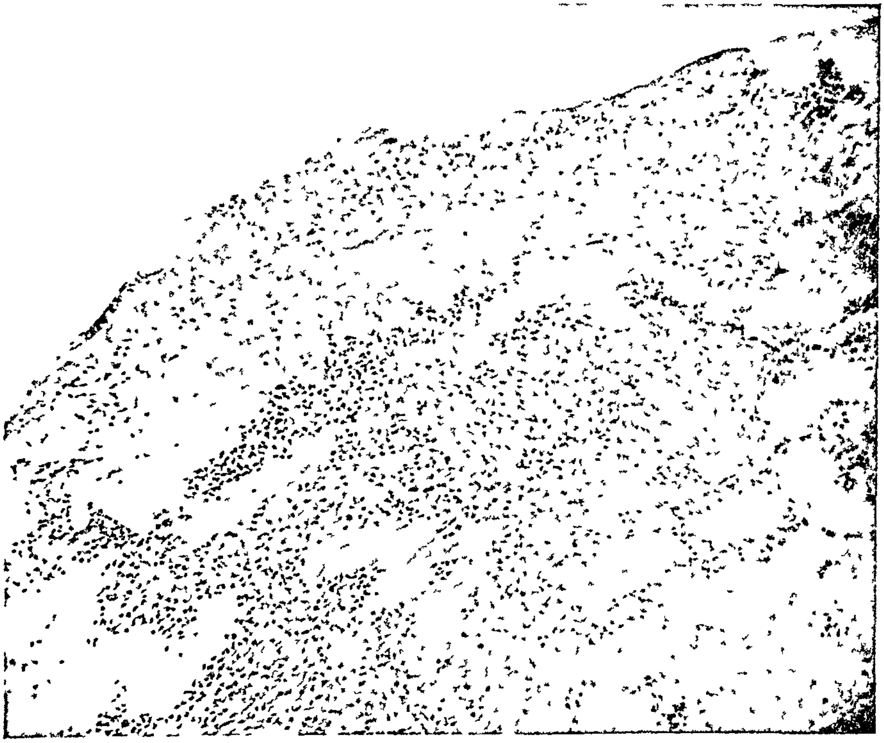

Fig 4 —Photomicrograph of the plug of tissue removed from the esophageal orifice of the fistulous tract Note the necrotic tissue membrane with a large number of inflammatory cells, bacterial colonies, and some squamous cells

of the fistula was edematous and inflamed but without frank pus Microscopic examination of this tract showed a necrotic tissue membrane with many inflammatory cells, frequent bacterial colonies, and a few squamous cells (Fig 4) Cultures of the specimen showed a coagulase positive *Staphylococcus aureus* Other findings were situs inversus and a stomach filled with blood

DISCUSSION

Barrie and Townrow,[1] in a review in 1946 of the literature of aortic esophageal fistula, found 80 reported cases Since that time other cases have been added[2,3] These reports indicate that the following features are quite constant The perforation has been caused usually by a sharp object, often a fish or rabbit bone, which probably accounts for the larger number of cases reported from the British Isles where such foods are common The aorta has been the great vessel most frequently involved due to its proximity to the area of the esophagus where foreign bodies often lodge After the ingestion of a foreign body, chest pain occurred in the majority of cases, receded for a variable time but generally returned before death from hemorrhage A striking fact is the regularity with which a fatal hemorrhage has been preceded by a signal hemorrhage Barrie and Townrow[1] in presenting 18 well documented cases observed that all exhibited such signal hemorrhage The interval averaged 1 day and ranged from 2 hours to 3 days In our case, the first evidence of bleeding was 7 days prior to death Spasm of the arterial wall closing the orifice, hypotension from hemorrhage, and occlusion of the fistula by clots, later digested with infection, have been offered as reasons for the latent period

The sequence of events in the formation of such fistulas may follow this pattern The esophagus is perforated by a sharp object at the aortic arch level with leakage into the mediastinum The sharp end may either injure the aortic wall or completely traverse it, as in our case The foreign body may pass through the alimentary tract spontaneously or be removed surgically Sepsis follows in the wall of the esophagus and aorta and surrounding area A fistula then evolves from infection and abetted, perhaps by digestion from esophageal contents The initial bleeding may exert some tamponade effect only to recur as a fatal and massive hemorrhage with further progress of infection and digestion We have not found in the literature any case of established aortic esophageal fistula which has been successfully treated Even if the diagnosis were established after the signal hemorrhage, with the fistula already established, surgical treatment in the presence of such infection would be a challenging problem In anticipation of this entity the best approach seems to be its prevention These suggestions are offered after the experience with this patient Foreign bodies of this type with significant symptoms indicative of possible injury to the aorta should be removed early through an open extrapleural approach if possible This is particularly true if serious symptoms and signs of mediastinitis are present The esophagus and aorta should be separated by the interposition of other tissues and the area drained Even though small the esophageal opening should be closed by sutures and the esophageal lumen drained by tubes with constant suction. Antibiotic therapy should be broad and massive in type and should be continued for a considerable time.

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A PULSATING EPIGASTRIC MASS DUE TO PERFORATION OF A TUBERCULOUS PERICARDIAL ABSCESS THROUGH THE DIAPHRAGM

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PERICARDIAL cysts and diverticula appear radiographically as projections from the cardiac silhouette, but a definite diagnosis is not commonly established prior to thoracotomy. They may be asymptomatic or may cause pain, fullness in the chest, and cough.[1] Extensive anatomic derangement or destruction of neighboring structures rarely occurs. The only report of such a case was published by E. H. Cushing in 1937.[2, 3] His patient had a tuberculous pericardial diverticulum which dissected through the anterior chest wall. The present report concerns a patient who also had a tuberculous pericardial diverticulum or abscess that perforated the diaphragm and presented in the epigastrium as a pulsating mass.

CASE REPORT

J. A. O., a 50 year old textile worker, was admitted to the Durham Veterans Administration Hospital on Dec. 14, 1953, with the chief complaint of pain in his chest and abdomen. He had considered himself well until 11 weeks prior to admission when he had developed a "2 week cold" characterized by cough and left lateral pleuritic chest pain. He consulted his physician and was given symptomatic therapy. The cough subsided, but the pleuritic pain persisted and was associated with a constant dull pain along the left anterolateral costal margin which radiated into the epigastrium. After 2 weeks of continual discomfort, he again consulted his physician, and a pulsating mass was found in the epigastrium. The patient was hospitalized elsewhere. Fluoroscopic examination and x-ray studies, with the aid of induced pneumoperitoneum, revealed a pulsating 15 cm. bilobular mass in the epigastrium. The patient declined surgical exploration and returned home to bed rest. Due to persistence of pain, the patient again sought medical attention and was admitted to the Durham Veterans Administration Hospital.

The patient denied having had any chest pain prior to his present illness and had no known contact with tuberculosis. He denied having had fever, chills, or night sweats, but had lost approximately 10 pounds in weight during his present illness. There was no past history of hypertension, syphilis, intermittent claudication, or symptoms of congestive failure

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Physical examination revealed a temperature of 98° F., blood pressure 90/60 mm. Hg, a pulse rate of 96, and a respiratory rate of 16. Fremitus, resonance, and breath sounds were diminished at the left lung base. The heart was not enlarged laterally to percussion.

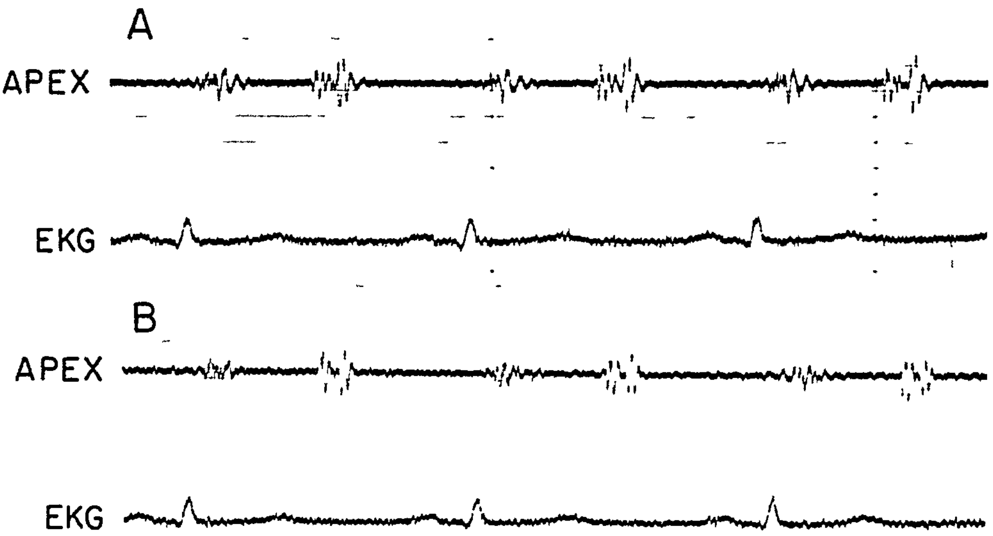

Fig. 1.—Phonocardiogram of apex. *A* is control and *B* is with application of pressure to the epigastric mass.

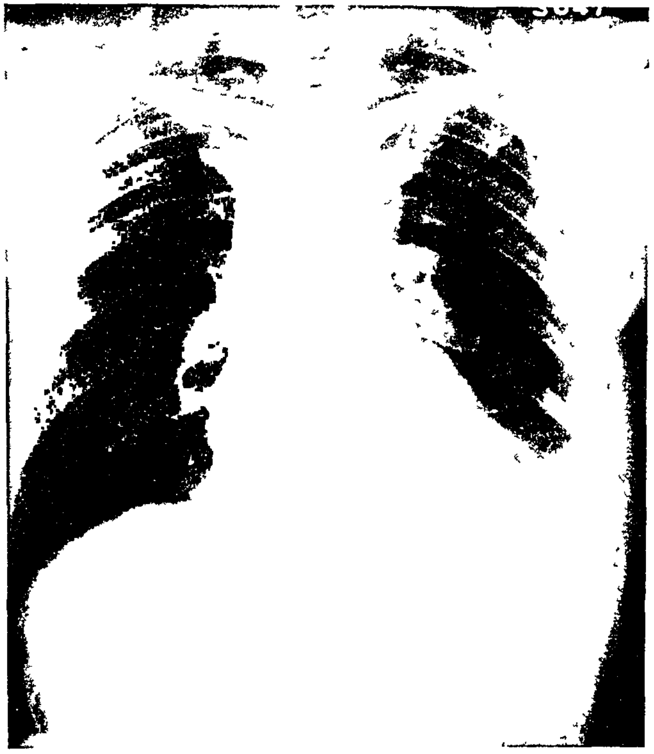

Fig. 2.—Roentgenogram of the chest on admission to the hospital.

No murmurs were heard over the precordium. The aortic and pulmonic second sounds were of equal intensity. The second sound at the apex was split. There was a 9 to 10 cm. mass in the epigastrium which pulsated paradoxically with ventricular contraction, the expansion occurring before the carotid and femoral pulsation. The mass was dull to percussion and blended into the area of cardiac dullness. A murmur could not be heard, but there was a transmission of the second sound from the cardiac apex over the mass. The splitting of the second sound could be obliterated by exerting pressure on the mass (Fig 1). No murmur could be heard posteriorly. The liver, spleen, and kidneys were not palpable. There was no venous distention and peripheral pulses were normal.

The Kahn test was negative. White blood cell count was 7,400 with a normal differential. Hemoglobin was 12.5 grams per cent and the sedimentation rate (Wintrobe) was 51 mm per hour. Urinalysis was normal. A roentgenogram (Fig 2) revealed a left pleural effusion, but a parenchymal lesion could not be seen. Thoracentesis confirmed the presence

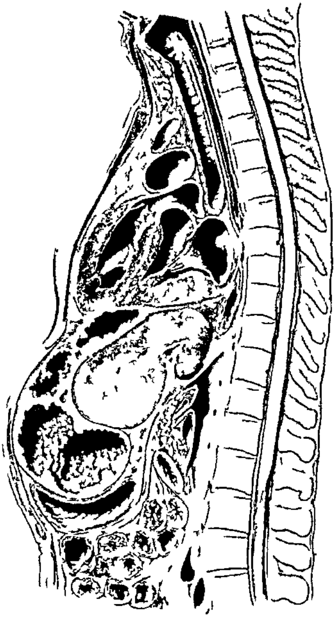

Fig 3.—Artist's concept of the pericardial abscess perforating diaphragm shown in midplane sagittal section. The abscess is below the heart, extends in front of the liver, displaces the stomach down and produces the epigastric protuberance.

of a pleural effusion, the fluid being cloudy and straw colored in appearance. The specific gravity was 1.019 and there were 4,425 white blood cells per cubic millimeter of which 90 per cent were mononuclear cells. Protein content of the fluid was 5.4 grams per cent. No tubercle bacilli could be demonstrated by either stain or culture. The cells were classified as Papanicolaou Type III. First strength tuberculin PPD skin test was positive. The electrocardiogram showed a horizontal axis and T wave changes consistent with left ventricular ischemia. X-ray studies of the abdomen, including planigraphy and studies before and after induced pneumoperitoneum, revealed a well-outlined epigastric mass which was noncalcified and caudad to the diaphragm.

At surgical exploration on Dec 31, 1953, the abdominal cavity was entered through an upper midline incision. A pulsating mass was encountered which was not attached to the anterior parietal peritoneum and appeared to be covered with a layer of peritoneum. Pulsations were synchronous with ventricular contraction and quite distinct from pulsations of the abdominal aorta. The mass was adherent to the dome of the liver but could be separated readily by blunt dissection (Fig. 3). As the mass appeared to arise from above the diaphragm, the incision was extended into the left thorax through the eighth interspace. As the pleura was opened, the pleura and pericardium were seen studded with tubercles; the pleura was biopsied. The mass appeared to arise from the pericardium, displacing the anterior leaf of the diaphragm with a ventral perforation through this structure. At the point of perforation, the mass was approximately 6 cm. in diameter and no communication with the pericardial space could be demonstrated. Needle aspiration revealed thick, yellow, purulent material. The chest incision was closed, and the lower half of the abdominal incision was also closed so that the mass could be isolated from the peritoneal space. Approximately 500 c.c. of thick, yellow pus was drained, cultures of which subsequently yielded tubercle bacilli. Drains were placed in the abscess cavity, and the upper portion of the abdominal incision was left open. The patient was started on chemotherapy receiving 300 mg. of isonicotinic acid hydrazide (INH), 12 Gm. para-aminosalicylic acid (PAS), and 2 Gm. streptomycin daily from Dec. 31, 1953, until Jan. 29, 1954, when PAS was discontinued and streptomycin reduced to 1 Gm. twice weekly. The postoperative course was uneventful. By the end of 6 weeks the abscess cavity had completely healed and the electrocardiogram returned to normal. On April 14, 1954, the patient was sent home on modified bed rest with instructions to continue chemotherapy.

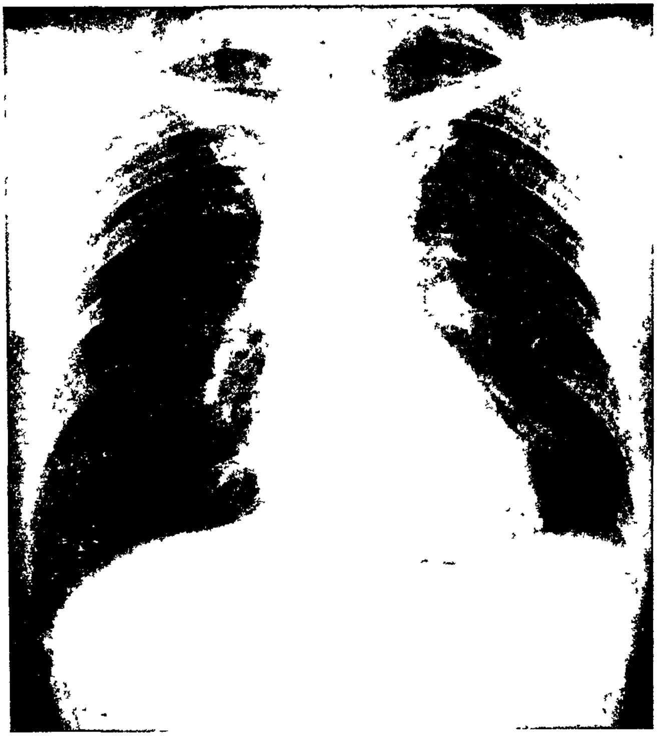

Fig 4.—Follow-up roentgenogram of the chest.

Following discharge from the hospital, the patient continued to do well and remained symptom free. Streptomycin was discontinued in January, 1955, and INH in June, 1955. In September, 1955, a roentgenogram (Fig. 4) and electrocardiogram were normal, and the patient had returned to work. Our last communication was in April, 1958, at which time he was asymptomatic and working full time.

DISCUSSION

Hart[4] reported the first pericardial projection in 1837 Subsequent reports have suggested that such projections may represent a true pericardial hernia, a coelomic cyst, a congenital pericardial diverticulum, or an acquired or inflammatory pericardial diverticulum [2-9] A true pericardial hernia has been described as a protrusion of the serous membrane through a defect in the fibrous membrane of the pericardium [10] Coelomic cysts are thought to represent a persistence of the ventral parietal recess of the pericardial coelom [11] They are usually located at the right cardiophrenic angle and do not communicate with the pericardial space While some authors consider pericardial diverticula as congenital in origin, others believe that they result from inflammatory processes [2, 6, 8, 10, 13]

Tubercle bacilli have rarely been demonstrated in pericardial diverticula Freedman[14] reported 2 such cases in 1937, but one of these had been previously reported by Cushing Eschbach[12] in his review erroneously referred to these as 3 cases

Tuberculosis, even with its protean manifestations does not often involve the muscle component of the diaphragm Tu,[15] in 1950, reported what was stated to be the second case of a tuberculoma of the diaphragm Lucke[16] describes caseous foci in the diaphragmatic muscle in military tuberculosis, and Tobias[17] reported immobilization of diaphragm with tuberculous involvement of the muscle of the diaphragm Auerbach[18] reviewed 209 cases of tuberculosis of serous cavities and described 11 instances of spread of tuberculosis through the diaphragm to the peritoneum via the lymphatics and 5 cases of spread from the peritoneum to the pleura by caseous foci through the wall of the diaphragm He did not record the occurrence of perforation of the diaphragm by a supradiaphragmatic tuberculous abscess Tuberculous abscesses of the peritoneal cavity, however, have been known to perforate the diaphragm [19]

SUMMARY

An inflammatory pericardial diverticulum or abscess of tuberculous origin that perforated the diaphragm and presented in the epigastrium as a pulsating mass is reported This report is of interest not only because of its rarity, but because it again demonstrates the destruction possible from an inflammatory pericardial abscess and describes an unusual type of epigastric mass

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A COMPLICATION OF THE HUFNAGLE VALVE

A Case Report

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NUMEROUS attempts to remedy the defects in the cardiac-valvular system produced by the many congenital, infectious, and degenerative processes of man have been made.[1, 2, 3] It is apparent that some degree of success has been achieved[4, 5] but inadequacy of the present techniques is evidenced by the constant new approaches to the problem.[6]

A recent case studied clinically and anatomically at this hospital demonstrated a postoperative complication that does not seem to have been previously reported.

CASE REPORT

A 28 year old white man had rheumatic heart disease with aortic insufficiency of such degree that surgical valve insert in the aorta was considered advisable. In May, 1956, the patient had a Hufnagle valve, plastic type, inserted in the descending thoracic aorta at another hospital. Recovery was excellent and the patient had one year of fairly normal life.

In May, 1957, he was admitted to this hospital with signs and symptoms of a left femoral artery embolus. An embolectomy of the left femoral profunda artery was performed. He was discharged on anticoagulants and did well. In June, anticoagulants were discontinued. In September, 1957, pain in the left calf was noted but palpable pulses and warm extremity were present. Arteriogram showed definite narrowing at site of previous embolectomy. He was discharged with the advice that a bypass operation would be performed if pain persisted.

In April, 1958, acute sudden pain developed, associated with numbness and coldness of the left leg. Dorsalis pedis and posterior tibialis pulses were absent on the left. Conservative management was administered. He recovered fairly satisfactorily with some residual claudication and was sent home on leave. On July 27, 1958, while on leave, sudden acute right leg pain was experienced. The right femoral pulse was good but dorsalis pedis and posterior tibialis vessels were without pulse. The right leg was colder than the cool left one. An aortogram showed occlusion of left common iliac at its bifurcation. A right femoral arteriogram showed occlusion of a segment of the right popliteal artery with fair filling below. On Aug 7, 1958, a right popliteal artery embolectomy was performed. Anticoagulants were administered. Recovery from this operative procedure was uneventful.

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Microscopic studies of the valve ball demonstrated an organized laminated thrombus without evidence of any bacterial growth or inflammatory reaction surrounding it. Sections through the embolus in the left femoral artery showed a well-organized portion at the origin of the profunda branch with a more recent thrombus above this site. Blood cultures were negative for bacterial growth.

CONCLUSIONS

Although artificial valves hold great promise in the surgical treatment of those who have valvular defects, one must select the material of which they are made very carefully. In addition, long-term follow-ups will be necessary to assay the hemodynamic consequences and deteriorative tendencies of such prostheses. In this case, the laminated plastic material finally broke down with resultant split in the surface. At this site, the ball developed a thrombus. Multiple emboli broke off from the thrombus with resultant peripheral arterial occlusion. The laminated hollow ball proved undesirable in this case because it split with resultant thrombus formation.

SUMMARY

A thrombus formed in a 28-year-old white man as a result of splitting of the lamina in the plastic ball of a Hufnagle valve. Multiple emboli from this artificial valve thrombus occurred over a period of 1½ years. Emboli in patients with artificial valves must be carefully considered as potentially arising from the valve.

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A SIMPLE OVERHEAD STERNUM RETRACTOR

John Storer, M.D., and Edward R. Malia, M.D., Cleveland, Ohio

Retraction of the sternum during the surgical attack on certain cardiac lesions has formerly required the concerted effort of one assistant. This, of course, applies only to the incisions making use of a transverse sternotomy. It is our practice in most cases requiring total body perfusion to make a bilateral submammary incision through the fourth intercostal space, and to transect the sternum in V-shaped fashion. We have used a variety of retractors to spread the interspaces but all have the disadvantage of displacing the inferior portion of the thoracic cage along with the inferior portion of the transected sternum in a posterior direction. This exerts an undue amount of pressure on the myocardium and visibly affects the cardiac action. It is extremely inconvenient for an assistant to maintain continuous traction on this portion of the sternum and almost impossible over a prolonged period to keep the sternum off of the myocardium. It therefore occurred to one of us (E. R. M.) that two hooks could be inserted around the fifth rib, just lateral to the sternum, and suspended from an overhanging pulley. This implement has been used in the last 20 procedures which required this type of incision. It has proved to be completely satisfactory. The cord which is attached to the sternal hooks does not interfere with the surgical technique in any way.

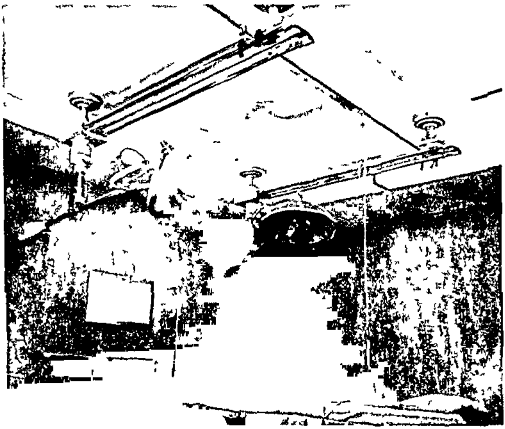

Fig. 1.—Sternum retractor assembly suspended over operating table.

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This retractor is arranged in our operating room by fixing a metal shaft to the two parallel supports for the American sterilizer dual video lights (Model D-V 22). A simple pulley and stout cord are then sterilized and just preparatory to surgery one of the completely gowned assistants fastens the pulley and cord to the overhanging rod The operating table is situated under this rod in such a manner that the pull on the hook will be at about a 10-degree angle toward the feet. The cord is tied into a small bundle and left suspended in the air until that point in the operative procedure is reached when sternal retraction is necessary. Then the hooks are inserted under the fifth ribs on either side of the sternum and the cord passed through a ring which supports the hooks Traction is made on the cord sufficiently so that the sternum is elevated to the required amount. Two large clamps are placed on the cords for fixation.

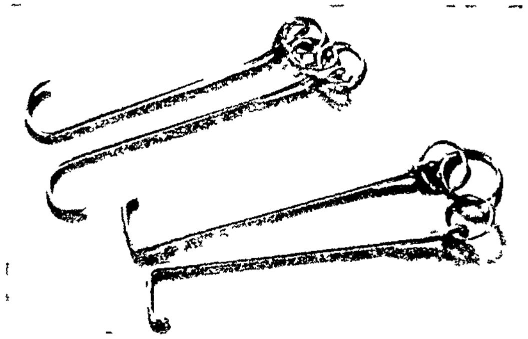

Fig 2 —Two types of hooks have been used

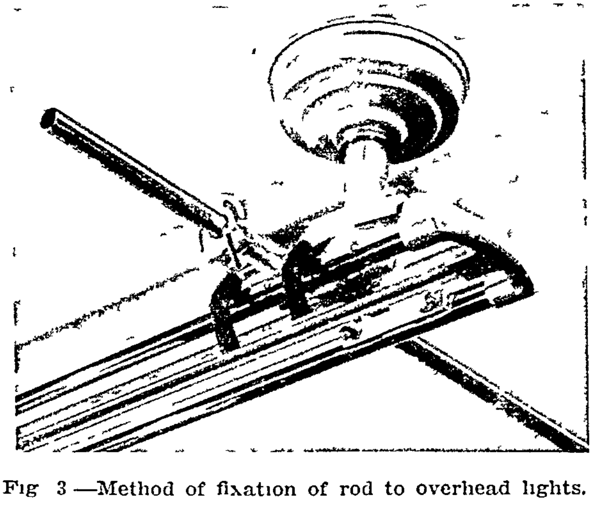

Fig 3 —Method of fixation of rod to overhead lights.

Accidental contamination of the cord, prior to sternal retraction, occurred following manipulation of the overhead lights the first time it was used. This has been controlled by familiarity with the presence of the cord and delegating to one circulating nurse the complete responsibility for all manipulation of the overhead lights.

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PHYSIOLOGIC STUDIES DURING HIGH FLOW, NORMOTHERMIC, WHOLE BODY PERFUSION

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Whole body perfusion for open intracardiac operations may be accomplished by a variety of techniques. Experience has led to the evolution of the system of high flow, normothermic perfusion which has been employed in this institution and found to be clinically satisfactory. The purpose of this study is to document the effect of such a perfusion upon certain physiologic variables in the perfused subject.

MATERIAL

During the last 2 weeks of August, 1958, 3 patients having acyanotic congenital heart disease were selected for study from the operative schedule of the Mayo Clinic.

Case 1 was that of a 10-year-old girl whose only symptom was easy fatigability. She weighed 36 kilograms and had a body surface area of 1.24 square meters. There was no precordial thrill, and the systolic murmur was only moderately loud. The heart was not enlarged. Cardiac catheterization performed elsewhere had indicated the presence of both atrial and ventricular septal defects. At operation on Aug. 19, 1958, an atrial septal defect was re-

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paired, but ventriculotomy and careful search revealed an intact ventricular septum. Her recovery was uneventful, and she was dismissed from the hospital 9 days later. A very faint residual systolic murmur could be heard.

Case 2 was that of a 9-year-old boy who had had fatigability and dyspnea on exertion throughout life. He weighed 41 kilograms, and his surface area was 1.24 square meters. His heart was overactive. He had a precordial thrill and an extremely loud systolic murmur. The heart was enlarged and the pulmonary vascular markings prominent. At operation on Aug. 26, 1958, the right ventricular systolic pressure was 45 mm. Hg. A typical high ventricular septal defect was identified and repaired by direct suture. His recovery was uneventful and he was dismissed from the hospital 11 days later, with no residual murmur audible.

Case 3 was that of a 9-year-old boy who had been slow to gain weight and who always seemed tired in spite of limited activities. He weighed 23 kilograms, and his surface area was 0.92 square meter. There was no precordial thrill, but a harsh systolic murmur and a markedly accentuated second pulmonic sound were present. The heart and pulmonary-artery segment were large at the time of operation (Aug. 28, 1958), and the right and left ventricular pressures were equal. A large patent ductus was identified and doubly ligated. A typical high ventricular septal defect was repaired by direct suture. Following perfusion, the right ventricular systolic pressure was normal (30 mm. Hg). The postoperative course was smooth, and the patient was dismissed from the hospital in 12 days, at which time no murmurs could be heard, although the second pulmonic sound remained somewhat accentuated.

METHOD

Anesthesia was induced with thiopental sodium and maintained with a mixture of 70 per cent nitrous oxide and 30 per cent oxygen at high flows, augmented as required with small doses of succinylcholine administered intravenously. Exposure for the operation was obtained through a bilateral anterior thoracotomy. Cannulation methods were those described previously.[1] A Gibbon-Mayo pump-oxygenator was used.[2, 3]

The rate of blood flow during perfusion was anticipated on the basis of previous experience, utilizing a system of perfusion wherein the rate of blood flow was controlled entirely by the rate of venous return. That experience indicated that when venous cannulation is perfect, and the patient normothermic, the perfusion rate is approximately 2.4 L. per minute per square meter of body surface[4] in the small child, diminishing to 2.0 L. per minute per square meter for an adult. Therefore, for children of the size selected for the present study, a flow of approximately 2.3 L. per minute per square meter of body surface was anticipated.

The pump which propels venous blood to the top of the oxygenator (the oxygenator pump) was set before the perfusion to deliver blood at this rate. The output of the arterial pump is regulated by level-sensing devices to equal the rate of venous blood return from the patient, up to a maximum that equals the output of the oxygenator pump. Venous return exceeding this volume per minute accumulates and is sequestered in the venous reservoir and such blood is called "venous reservoir excess" Such excess usually accumulates after the heart is opened and the intracardiac blood is aspirated, and is thought in the main to represent central blood volume If venous return should diminish later in the perfusion as a result of surgical hemorrhage, the excess blood in the venous reservoir will be returned automatically by the machine to the circulation Under these circumstances, transfusion of a similar amount of blood will be required at the end of the perfusion when the central compartment is refilled

There was no recirculation of blood through the oxygenator during total perfusion A gas mixture consisting of 10 L of oxygen and 0 2 L of carbon dioxide was passed through the oxygenator each minute

Normal body temperature is maintained in the perfusate by incorporating in the pump oxygenator a heat exchanger of the type developed by Brown and his colleagues[5] The oxygenator pump moves blood through the heat exchanger before it reaches the oxygenator

Body temperature was measured by means of a thermistor passed transnasally into the mid esophagus

Venous pressure was measured by a plastic needle placed percutaneously into the left external jugular vein and by another placed in the right saphenous vein at the ankle These were connected by nylon tubing to strain gauge manometers which activated appropriate apparatus for permanent recording of the pressure tracings on photographic paper[6] Similarly, arterial pressures were recorded by means of a small catheter passed 6 inches proximally through a needle placed percutaneously into the right femoral artery Appropriate measurements were then made from the developed photographic paper The mean venous pressure is here considered to be the average of the external jugular and the saphenous mean pressure

A tachometer that measured the rate of rotation of the arterial pump recorded on the same photographic paper From this information, the rate of blood flow through the extracorporeal circuit was determined The output of the arterial pump was calibrated following each perfusion against pressures equal to those occurring during perfusion in the arterial line leading to the patient The pressures generated in this arterial line were measured by a manometer system which is connected by a side arm to the arterial line

Values for total peripheral resistance expressed in dynes seconds centimeters[5] were obtained by application of the formula

$$\text{total peripheral resistance} = \frac{(\text{mean arterial} - \text{mean venous pressure in mm Hg}) \times 1{,}332 \times 60}{\text{blood flow in liters per minute} \times 1{,}000}$$

Blood samples used in the study of acid base balance were drawn from an artery of the patient or the arterial line of the machine into sterile syringes, the dead space in the syringes having been filled with undiluted heparin solution which prevented clotting and enabled the procurement of blood samples free of air bubbles The syringes were immediately capped and placed in ice, and the samples were analyzed without delay for plasma carbon dioxide content, plasma pH, and erythrocytic volume percentage (hematocrit reading). Plasma carbon dioxide was determined on blood centrifuged after the method of Davenport[7] and analyzed by the method of Van Slyke and Neill.[8] Plasma pH was determined in a glass electrode assembly (Cambridge research model pH meter) enclosed in a circulated water jacket and maintained at 37° ± 0.1° C. For hematocrit determinations, blood was centrifuged in Wintrobe-Magath tubes at 1,500 revolutions per minute for 20 minutes. From these data, values for the partial pressure of carbon dioxide in the plasma and for the buffer base in whole blood were derived from the nomogram of Singer and Hastings.[9]

At about the mid-point of each perfusion, samples of whole blood were obtained from the venous and arterial lines of the bypass apparatus for the determination of oxygen content and oxygen capacity by the method of Van Slyke and Neill.[8] Oxygen consumption was then calculated from the formula: oxygen consumption = blood flow rate × (arterial blood – venous blood oxygen content). The error in this determination, resulting from the fact that bronchial arterial blood flow returns directly to the heart, is estimated to be negligible in these patients.

Oxygen tension of arterial blood was determined by the polarographic method,[10*] utilizing a sterile Clark oxygen electrode introduced directly into the flowing blood column in the arterial line of the bypass apparatus.

Percentage saturation of hemoglobin with oxygen was calculated after correcting for dissolved oxygen by dividing the oxygen content of the sample by its oxygen capacity. Dissolved oxygen content in the arterialized samples was calculated from two factors: the oxygen tension (pO_2) observed at the appropriate oxygen electrode at the time the sample was withdrawn, and the solubility coefficient for whole blood (0.023 c.c. of oxygen per cubic centimeter of solution at a pO_2 of 760 mm. Hg at 37° C.).[11] In the samples of venous blood, dissolved oxygen content was assumed to be 0.12 volume per 100 c.c. (that is, having a pO_2 of 40 mm. Hg).

RESULTS

Figs. 1, 2, and 3 record the arterial and venous pressures, flow rates, total peripheral resistances, venous reservoir excesses, and transfusions required during the perfusions in the 3 patients, respectively.

Mean arterial blood pressure dropped significantly (10 to 30 mm. Hg) at the time perfusion was begun, but during perfusion there was a definite small increase in the mean arterial pressure in 2 of the 3 cases. Total peripheral vascular resistance also increased during the period of perfusion in these 2 patients, but dropped significantly in all 3 patients at the instant cardiac asystole was relinquished.

The mean venous blood pressure remained essentially constant throughout each of the perfusions. The rate of blood flow during total perfusion was likewise constant in each of the cases, being approximately 2.3 L. per minute per square meter of body surface The excess volume of blood above that which was required to maintain these blood flows was automatically withdrawn from circulation into the venous reservoir, as is also demonstrated by the graphs During intracardiac repair the attendant surgical blood loss led not only to the gradual automatic return of this sequestered blood to the circulating volume but also required the transfusion of additional heparinized blood, amounting to about 600 c c in each instance

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*These determinations were made by Dr. Manly Levin during the course of more extensive studies relating to blood oxygen tensions during perfusion.

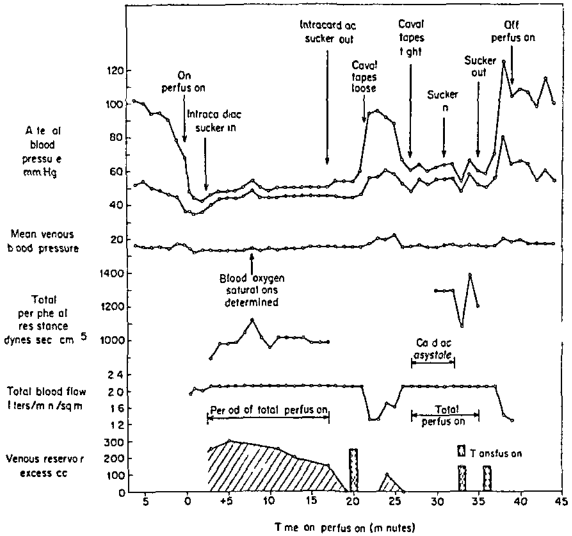

Fig 1 —Hemodynamic data recorded during perfusion in Case 1

In Table I are recorded the sizes of the arterial and venous cannulas used in the three patients, together with the blood flow rates employed, and the pressures that developed on either side of the cannulas From this information, the pressure gradients across the cannulas were computed For the venous cannulas this gradient varied from 20 to 26 mm Hg, and for the arterial, from 35 to 80 mm Hg

TABLE I CANNULA SIZE AND PRESSURE GRADIENT

		VENOUS CANNULAS				ARTERIAL CANNULAS			
SF	FLOW (L /MIN)	INTERNAL DIAMETER (INCHES)	VENOUS PRESSURE*	VENOUS RESERVOIR PRESSURE*	APPROX GRADIENT*	INTERNAL DIAMETER (MM)	ARTERIAL PRESSURE*	LINE PRESSURE*	GRADIENT*
1	2 6	5/16	13 to 16	-3 to -10	20	5 4	45 55	100 125	60 70
2	3 0	5/16	19 to 25	-3 to -10	26	5 4	45 85	105 160	60 80
3	2 1	5/16	13 to 19	-3 to -10	20	6 4	55 65	85 100	35 40

*In millimeters of mercury

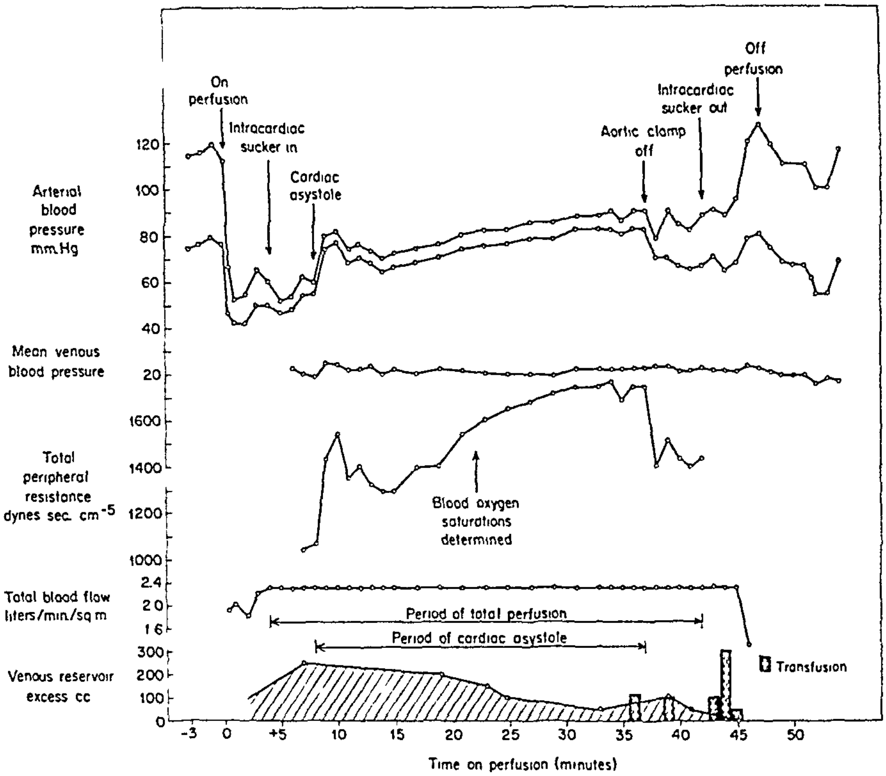

Fig. 2.—Hemodynamic data recorded during perfusion in Case 2.

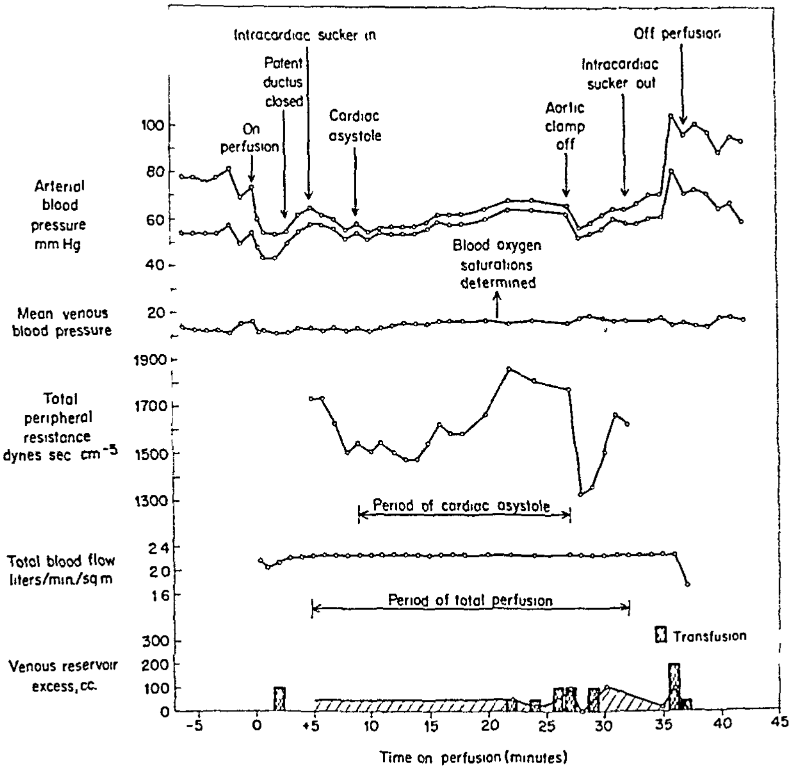

Fig. 3.—Hemodynamic data recorded during perfusion in Case 3.

Fig. 4 records the esophageal temperatures in each of the 3 cases. Although there was considerable variation in body temperature both before and after perfusion in these patients, the arterialized blood was constantly maintained during perfusion within the range of 36.5° to 37.5° C. After the beginning of perfusion, body temperature quickly equilibrated with the temperature of the perfusate.

Table II and Figs. 5, 6, and 7 record the acid-base balance that occurred throughout the operative procedure. It will be noted that the tension of carbon dioxide in the blood of the patients was markedly reduced by the hyperventilation associated with anesthesia and controlled respiration. Although some reduction in blood buffer base occurred during the course of anesthesia and operation, indicating accumulation of acid metabolites, the blood remained alkalotic owing to the overcompensation of hypocapnia. As perfusion is begun, mixing of the blood of the patient and the blood in the apparatus occurs. This mixing has been indicated by the cross-hatched zones on the graphs. The value for buffer base, which represents an accurate index to metabolic factors affecting acid-base balance,[9] dropped slightly during two of the three perfusions, and climbed in the third.

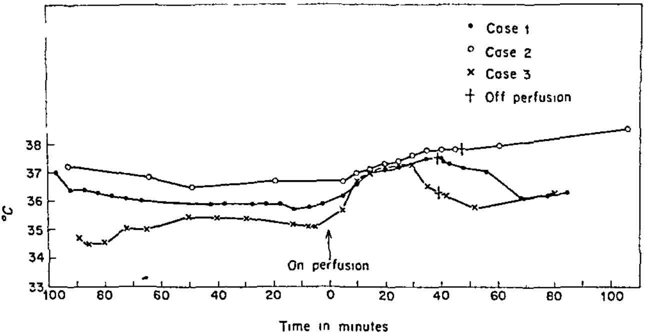

Fig. 4—Esophageal temperature of the 3 patients during operation

Blood for the final determination relating to acid-base balance was drawn just after completion of the operation, following extubation of the patient, and some time after spontaneous respiration had been resumed. This accounts for the high concentration of carbon dioxide and low pH at that time, but is not indicative of increased metabolic acidosis, as is evident from the stable level of buffer base. Although no determinations were made between the time of completion of perfusion and the time of completion of anesthesia, the dotted lines on the graphs are indicative of the supposition that resumption of controlled hyperventilation following perfusion again caused reduction in the partial pressure of carbon dioxide in the blood.

The percentage saturations of hemoglobin in venous blood returning from the patient and in arterial blood returning to him at about the mid-point of the

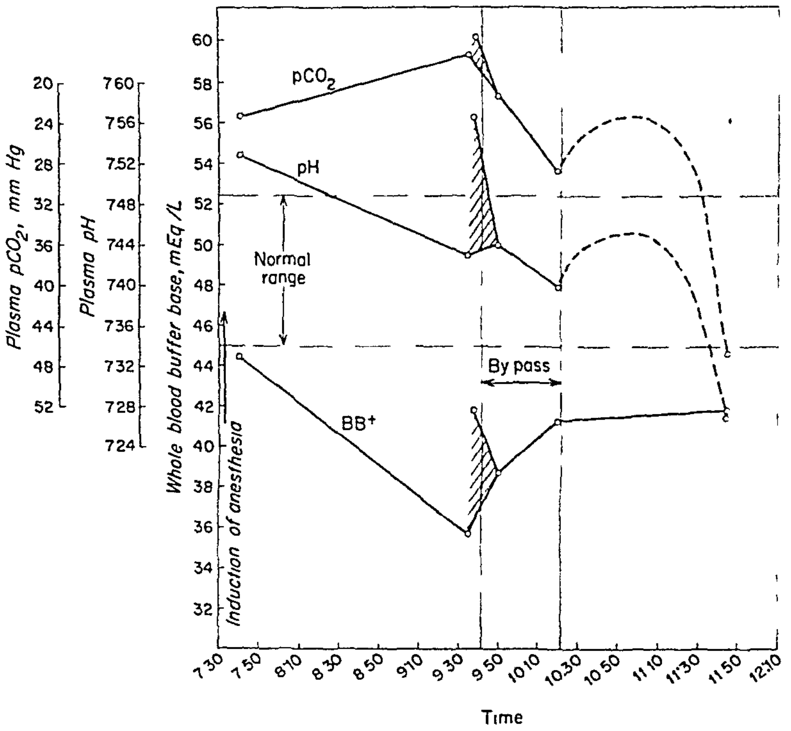

Fig. 5.—Acid-base balance occurring throughout the operative procedure in Case 1.

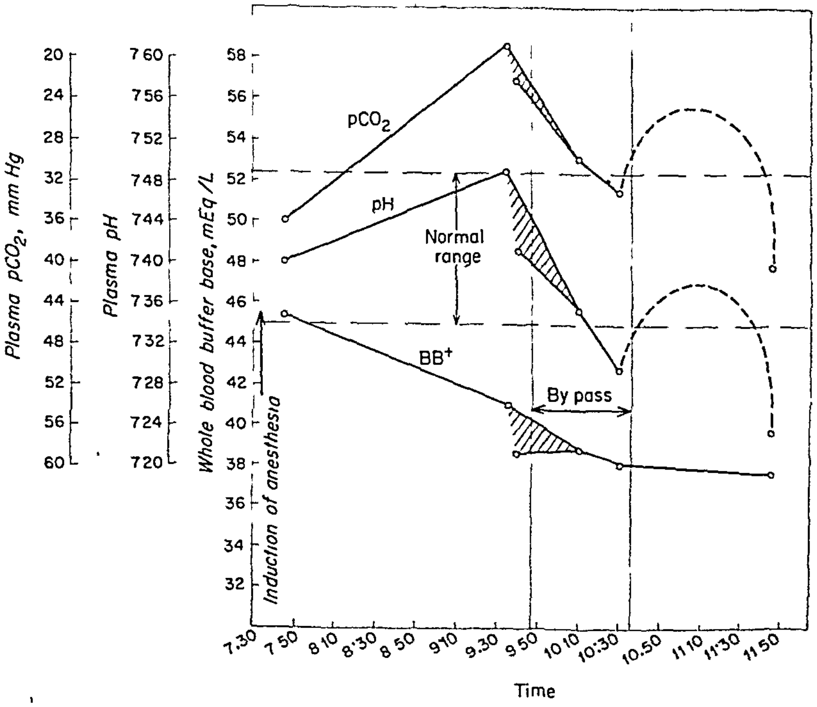

Fig. 6.—Acid-base balance occurring throughout the operative procedure in Case 2.

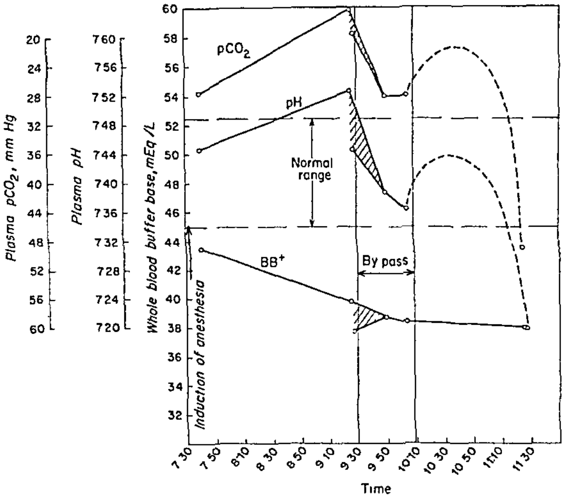

Fig 7.—Acid base balance occurring throughout the operative procedure in Case 3

Table II Acid Base Balance

CASE	SAMPLE*	HEMATOCRIT READING (RBC VOL %)	CO₂ (mM/L)	PLASMA pH	BUFFER BASE (mEq./L)	pCO (MM /Hg)
1	1	38.0	S† 19.85	7.528	44.5	23.4
	2	36.5	S 11.51	7.429	35.7	17.2
	3	42.0	S 13.88	7.545	41.7	15.7
	4	39.0	b† 12.41	7.438	38.8	21.4
	5	—	S 15.26	7.397	41.2	28.8
	6	40.0	S 19.51	7.267	41.8	47.0
2	1	43.0	S 22.82	7.400	45.3	36.0
	2	42.5	S 14.65	7.489	41.0	19.0
	3	—	S 14.63	7.410	38.6	22.2
	4	37.5	b 14.75	7.351	38.8	30.0
	5	41.0	S 16.87	7.295	38.0	33.0
	6	40.5	S 18.09	7.233	37.6	40.8
3	1	39.5	S 19.71	7.447	43.5	27.7
	2	39.0	S 13.39	7.526	39.8	16.3
	3	35.0	S 13.89	7.445	37.7	19.7
	4	37.5	b 14.48	7.386	38.7	27.9
	5	37.5	S 16.36	7.363	38.4	28.0
	6	44.0	S 20.37	7.200	38.0	49.0

*Identification of samples (arterial blood)

1 From patient just after induction of anesthesia
2 From patient just prior to onset of perfusion
3 From machine just prior to onset of perfusion
4 *From machine during perfusion*
5 From machine just prior to termination of perfusion
6 From patient at completion of operation just after extubation of patient

†S = plasma b = whole blood

perfusion are recorded for each of the cases in Table III. The average oxygen saturation of venous blood was 68 per cent, and complete arterialization was routinely accomplished by passage of the blood through the oxygenator. In two perfusions the hemoglobin of the arterial blood was completely saturated with oxygen, but excessive quantities of oxygen were not present in physical solution as demonstrated by satisfactory levels of oxygen tension (not in excess of 230 mm. Hg). Oxygen consumption during perfusion varied among the 3 cases from 100 to 162 c.c. per minute per square meter of body surface.

TABLE III. OXYGEN TRANSPORT DURING PERFUSION

	FLOW (L./MIN. /SQ. M.)	VENOUS BLOOD			ARTERIAL BLOOD				O_2 CONSUMPTION (C.C./ MIN./SQ. M.)
ASE		CONTENT (VOL. %)	CAPACITY (VOL. %)	SAT. (%)	CONTENT (VOL. %)	CAPACITY (VOL. %)	SAT. (%)	pO_2 (MM. HG)	
1	2.1	11.39	16.14	72	15.58	16.14	97	230	100
2	2.4	10.32	16.27	64	16.77	16.27	100+	135	162
3	2.3	11.49	16.69	69	17.06	16.69	100+	190	140

COMMENT

With the flow rates utilized in the system of perfusion here studied, mean arterial pressure at the onset of perfusion was subnormal. A tendency to gradual increase in peripheral vascular resistance resulted in a similar tendency for gradual elevation of mean arterial pressure during perfusion, so that in 1 patient (Case 2) it was near normal at the end of the perfusion. In a previous study reported from this clinic,[12] during perfusions with lower rates of blood flow, similar changes in arterial pressure and resistance were noted. Dodrill and colleagues[13] noted the same phenomenon, and Mendelsohn and associates[14] found subnormal mean arterial blood pressures during perfusion.

It has been amply demonstrated in dogs[15-18] that arterial blood pressure during perfusion is closely related to blood flow rates. On the basis of the arterial blood pressures maintained during the perfusions of the present study, the flow rates utilized (approximately 2.3 L. per square meter of body surface per minute) might be assumed to be less than the cardiac output of the anesthetized patient prior to perfusion. However, data for comparison of peripheral resistance before and during perfusion in these patients are not available and it is therefore not possible to eliminate reduction of peripheral vascular resistance during perfusion as being etiologic in the lowering of arterial pressure.

A steady rate of blood flow in this system of perfusion is dependent upon free and unobstructed venous return from the patient, as is accomplished by the use of the largest possible venous cannulas. This in turn has resulted in the nearly steady levels of venous pressure encountered during these perfusions. Venous cannular obstruction would result in sequestration of blood in the obstructed venous bed, with resultant unaccountable loss of circulating blood volume and increased venous pressures.

The partial pressure of carbon dioxide during heart-lung bypass is largely controllable in most systems of perfusion through alteration in the rate of ventilation of the oxygenator and in the fractional concentration of carbon dioxide in the gas passing through the oxygenator. In the perfusions being studied, the partial pressure of carbon dioxide in the arterialized blood was routinely maintained at levels that were lower than normal. This seems desirable, since the hypocapnia tends to prevent spontaneous respiratory motion by the patient, yet is probably not sufficiently severe to cause extensive reduction of cerebral blood flow.[19]

The development of mild metabolic acidosis during general anesthesia is usual.[20] Further progression of metabolic acidosis should not occur during perfusion if adequate flow rates of fully oxygenated arterial blood are employed.[21] The present studies indicate that this system of perfusion causes no significant increase in metabolic acidosis above that occurring during preperfusion anesthesia.

Oxygen consumption before and after perfusion has not been determined in clinical cases, and control values for comparison with oxygen-consumption data during perfusion are therefore not available. The average oxygen consumption of the anesthetized patients in this study during perfusion is somewhat lower than that occurring under waking basal conditions,[22] but is comparable to the oxygen-consumption values found during high flow perfusions under experimental conditions by several investigators.[15-18] Available data may be interpreted as indicating that oxygen uptake of a subject on perfusion increases with increasing perfusion flow rates only to a certain point, beyond which it remains unchanged with further increases in flow. At this point, the rate of blood flow probably results in perfusion of the entire body, rather than limited parts of it. Further increases of flow beyond this point, while resulting in no increase in oxygen uptake, result in a smaller arteriovenous oxygen difference. Oxygen uptake in these 3 cases averaged 134 c.c. per square meter per minute. In another study,[23] of a larger group of patients undergoing identical perfusions at this clinic, oxygen uptake averaged 130 c.c. per square meter per minute. This is comparable to the data available on oxygen uptake in anesthetized intact man.[20] From this it is concluded that the entire body is perfused by the system of perfusion used for the patients in this study. Venous oxygen saturations were found to be slightly lower during these perfusions than in intact resting man, implying a slightly subnormal average oxygen tension in the tissues.

The data gained from this study indicate that the body can be maintained in a nearly normal acid-base balance and hemodynamic state during interruption of cardiac function as permitted by the technique of normothermic, high flow, whole body perfusion here employed.

SUMMARY

Three patients requiring open-heart operations for repair of uncomplicated congenital heart lesions were selected for detailed physiologic study during operation. A system of perfusion utilizing a Gibbon-Mayo pump-oxygenator and a steady rate of blood flow of approximately 2.3 liters per square meter of body surface per minute was employed.

Mean arterial blood pressure became subnormal at the start of perfusion but tended to return progressively toward normal as the result of an increasing peripheral vascular resistance. Venous pressure remained steady and at a satisfactory level. Large size of the venous and arterial cannulas permitted minimal pressure gradients across them.

Metabolic acidosis of mild degree, compensated by respiratory alkalosis, occurred as a result of general anesthesia and manual hyperventilation, but perfusion caused no appreciable further metabolic acidosis.

Oxygen consumption during perfusion was found to be within normal limits for anesthetized man, and the oxygen saturation of venous blood hemoglobin was only slightly subnormal. The blood was fully arterialized by passage through the oxygenator.

The rate of blood flow employed during these perfusions is believed to be nearly as great as the rate of blood flow maintained by the functioning heart of the anesthetized patient.

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RESPIRATORY CHARACTERISTICS OF EXTRACORPOREAL PUMP-OXYGENATORS

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THE PUBLISHED REPORT of the symposium on *Extracorporeal Circulation*[1] clearly shows that mechanical pump-oxygenating systems can be operated successfully in a variety of ways. Several specific examples of this general statement might be mentioned. Various mixtures of oxygen and carbon dioxide can be used as the oxygenating gas. Various gas flow rates can be used. The gas can be prewarmed or left cold before entering the oxygenator, and it can be saturated with water or left dry. As yet the barometric pressure of a given locality has not limited the use of the pump-oxygenating systems. Finally, patients with widely varying metabolic rates can be perfused.

The variety of operating methods in current use is so great that the unwary might conclude that the variables mentioned above are unimportant. He might even be led to choose one operating feature from successful center A, another operating feature from successful center B, etc. No doubt, he would be surprised to view his own catastrophic results when he had chosen the best features of each of the best cardiac centers. The above is probably a ludicrous example, but it should serve to emphasize the point that extracorporeal pump-oxygenating machines are complex multifactorial systems that are finitely influenced by each of the factors alluded to in the previous paragraph. A change in any one of these factors changes the partial pressures of oxygen and carbon dioxide in the gas phase of the oxygenator and, hence, of the blood.

The purpose of the present paper is to interrelate in quantitative terms the factors which define the respiratory characteristics of the artificial heart-lung apparatus when connected to a metabolizing organism. This will be done in an abstract or theoretical form. The first problem encountered, in writing such a paper, is choice of tools to be used for the presentation. Words are poorly suited to the function of communicating abstract, quantitative ideas. Equations often bring about such a condensation of thought that functional interrelations are lost. Graphic analysis or nomography is a tool that is especially suited to this type of analysis and is the method used in the present paper. Henderson[4] was the first to apply this method to biologic systems.

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Rahn and Fenn[6] have used the method more recently to analyze the complexities of aviation physiology. The present paper utilizes many of the types of graphs developed by Rahn and Fenn. If the reader desires a rigorous development of the graphs used here, he is referred to their comprehensive monograph.

The present analysis is divided into five sections so that the reader can focus his attention more sharply on specific goals. The first section is a glossary of the symbols used. These symbols may at first appear cumbersome, but they conform to the standard symbols outlined in the symposium for the "Standardization of Definitions and Symbols in Respiratory Physiology."[5] The second section defines those factors which determine the partial pressures of oxygen and carbon dioxide in the gas phase of the oxygenator. The third section defines those factors which determine the partial pressures or tensions of oxygen and carbon dioxide in the blood that is leaving the oxygenator. The fourth section develops the thesis that the proper perfusion rate is determined by the aerobic metabolism of the organism being perfused and, as a consequence of this, the factors which determine the venous blood oxygen tension are defined. Finally, these various factors are simplified as shown in Fig 16, to point out one possible combination of monitoring devices which can be used to perform an adequate perfusion. This is the system currently in use at the University of Colorado Medical Center, which is a product of the analysis in the present paper. In essence, Fig 16 shows that the arterial tension of CO_2 can be adequately followed by the continuous monitoring of arterial pH, and can be controlled by varying either the concentration of CO_2 or the rate of flow of gas through the oxygenator. The arterial O_2 tension can also be followed polarographically and can be controlled by varying the ratio of oxygen consumption of the patient to the blood flow rate. I hope that the above broad outline of the organization and goals of this paper will help the reader maintain perspective as he is led through the more tedious portions.

I GLOSSARY OF SYMBOLS

P_{O_2}—Partial pressure or tension of oxygen (mm Hg) without reference to phase

Pa_{O_2} and $P\bar{v}_{O_2}$—tension of oxygen in arterial and mixed venous blood, respectively

$P_{I_{O_2}}$, $P_{C_{O_2}}$, $P_{E_{O_2}}$—tension of oxygen in influent, oxygenating chamber, and effluent gases, respectively, i e, the gas entering the oxygenator and the gas leaving the oxygenator

F_{O_2}—the fraction that oxygen is of the total gas mixture

C_{O_2}—the content of oxygen in blood (vols %)

D_{O_2}—rate of diffusion of oxygen

CO_2 or H_2O—may be substituted for O_2 in any of the above symbols without changing any meaning other than the reference gas

V_{O_2} and V_{CO_2}—rates of oxygen consumption and carbon dioxide production, respectively

V_G—rate of total gas flow through the oxygenator

$\dot{Q}$B—Cardiac output or pump flow rate.
PB—barometric pressure.
So_2—percentage saturation of hemoglobin with oxygen.
R—the ratio at which CO_2 exchanges with O_2.
RB—the blood respiratory exchange ratio.
R.Q.—the ratio of carbon dioxide production to oxygen consumption—the respiratory quotient.
SoL.—solubility.
M.W.—molecular weight.
Ds—disc speed or revolutions per minute.

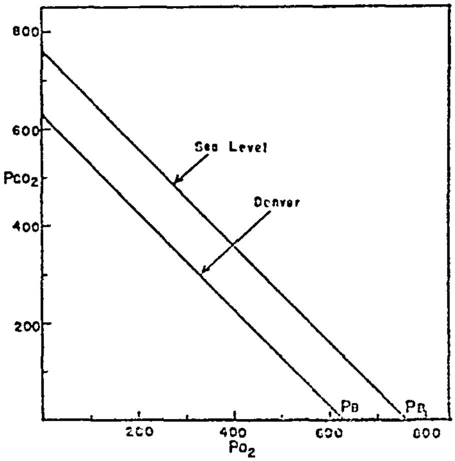

Fig. 1.

II. FACTORS CONTROLLING PARTIAL PRESSURES OF OXYGEN AND CARBON DIOXIDE IN THE GAS PHASE OF AN ARTIFICIAL OXYGENATOR

Most oxygenators operate with the gas phase at barometric pressure. In addition, most oxygenators handle only three gases: O_2, CO_2, and water vapor. Let us consider the consequences of these conditions. Dalton's Law states that the sum of the partial pressures of a mixture of gases is equal to the total pressure of the mixture. Since the total pressure is equal to the barometric pressure, we can write the following equation:

$$\mathrm{P_B = Po_2 + Pco_2 + P_{H_2O}} \qquad (1)$$

Now let us turn to Fig. 1 to begin the graphic development. The ordinate is the partial pressure of CO_2 in mm. Hg. The abscissa is the partial pressure of O_2 in mm. Hg. The possible extremes that could exist, in the system described, can be represented by a point on the Po_2 axis at 760 mm. Hg and by a point on the Pco_2 axis at 760 mm. Hg. The first point would represent dry 100 per cent oxygen at sea level. The second point would represent dry 100 per cent carbon dioxide at sea level. A straight line drawn between these two points completes a triangle which encloses all possible combinations of Po_2 and Pco_2 that can exist at a barometric pressure of 760. Denver, Colorado, is at an altitude of 5,280 feet and has an average PB of approximately 630 mm. Hg. The consequences of this fact are shown on Fig. 1 as the Denver line.

If we further limit the conditions under which the oxygenator operates, a more precise definition of Po_2 and Pco_2 can be achieved, since at 37° C, water vapor pressure is 47 mg If the oxygenating gas is saturated with water at 37° C, before entering the chamber, we can say,

$$PI_{H_2O} = PC_{H_2O} = PE_{H_2O} = 47 \text{ mm Hg} \qquad (2)$$

Substituting this into equation (1) and rearranging we have

$$P_B - 47 = Po_2 + Pco_2 \qquad (3)$$

or, for *Denver*

$$583 = Po_2 + Pco_2 \qquad (4)$$

This equation is expressed graphically in Fig 2 We begin with the Denver P_B line, subtract 47 from each of the coordinate points, and join them by a line This line, R, is the respiratory exchange ratio line If one substitutes any value between zero and 583, for Po_2 in (4), he can solve for Pco_2 If such points are plotted on Fig 2, it will be found that all points lie on the R line Therefore, the R line expresses all possible combinations of Po_2 and Pco_2 that can exist in the gas phase operating under the conditions specified (5,280 feet, water saturated, at 37° C) If the operating temperature is less than 37° C, the R line must be changed to correspond to the new P_{H_2O} value

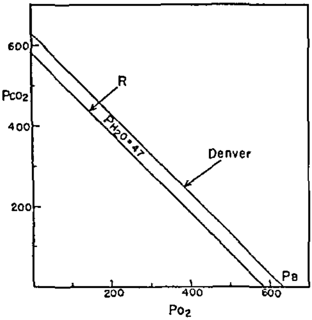

Fig 2

The next subject we shall consider is the factors that define the positions of the P_I, P_C, and P_E points on the R line The determination of the P_I point is the simplest and shall be considered first

Currently, most perfusionists use as an oxygenating gas either pure oxygen or a mixture of oxygen and carbon dioxide Thus, the minimum of carbon dioxide used is zero, and an average is about 3 per cent The maximum, to our knowledge, is 6 per cent These combinations in the influent gas mixture can be plotted on the R line of the $Po_2 - Pco_2$ diagram as shown in Fig 3 These points represent, in ascending order, zero, 3, and 6 per cent carbon dioxide Their positions on the graph are determined solely by the fractional concentrations of the influent oxygen and carbon dioxide

Now let us consider the definition of the Pc and Pe points. In the lungs, the magnitude of the difference between the alveolar point and the expired point on the R line is a direct function of the dead space. In the disc oxygenator the Pc point is analogous to the alveolar point in the lungs, and the Pe point is analogous to the expired point. The oxygenator has no dead space analogous to that in the lungs, so that in the oxygenator Pc = Pe.

Now we can proceed to analyze the two factors which define the difference between the Pi and Pc points on the R line. Fig. 4 is a $P_{O_2} - P_{CO_2}$ diagram with an expanded scale so that the influence of these two factors can be more readily appreciated. The reader will note that the Pi point is that of an oxygenator using pure oxygen. When this is true, the Pc point is completely independent of oxygen consumption, because removal of oxygen by the blood merely reduces the rate of flow of oxygen at the effluent end. However, as CO_2 escapes from the blood phase to the gas phase of the chamber, $P_{C_{CO_2}}$ increases and from (4) $P_{C_{O_2}}$ decreases. Or, from Fig. 4, the Pc point moves up the R line as a function of the rate of addition of CO_2 which, in a steady state, is the rate of CO_2 production by the organism being perfused. This ascent along the R line can be reversed by increasing the rate of total gas flow through the oxygenator. In essence, then, the difference between the Pi point and the Pc point is determined solely by the ratio of the total gas flow through the chamber to the CO_2 production, $\dot{V}_C/\dot{V}_{CO_2}$. Note that the right ordinate of the graph is expressed in these ratio units. For example, if an individual is producing 125 c.c. of CO_2 per minute, and there is an oxygen flow through the oxygenator of 5 L. per minute, he has a $\dot{V}_C/\dot{V}_{CO_2}$ of 0.04. His position on the R line is represented as point *C* on Fig. 4. This would yield a $P_{C_{CO_2}}$ of 22 and $P_{C_{O_2}}$ of 561. If the gas flow remained constant and the CO_2 production increased to 250 c.c. per minute, the $\dot{V}_C/\dot{V}_{CO_2}$ would decrease to 0.02 and the $P_{C_{CO_2}}$ would rise to 44. Having achieved this point the $P_{C_{CO_2}}$ could be returned to the original point, *C*, by increasing the gas flow to 10 L. per minute, thus restoring the ratio to 0.04.

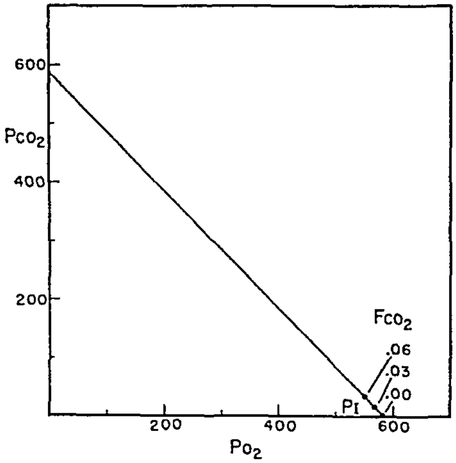

Fig. 3.

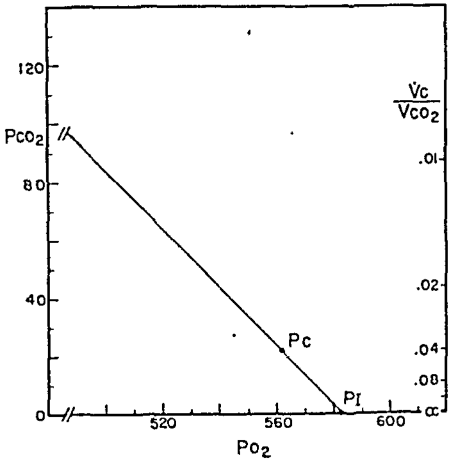

Fig. 4.

Fig. 5 is like the preceding diagram except in this case the influent gas contains 3 per cent CO_2. Note that having CO_2 in the oxygenating gas mixture shifts the Vc/Vco_2 lines up so that the infinity ratio coincides on the Y axis with the P_I point. Functionally, this means that for a given rate of CO_2 production, a higher rate of gas flow must be maintained to hold the chamber gas concentrations at a Pc_{CO_2} of 22 and a Pc_{O_2} of 561.

Now let us briefly retrace our steps before proceeding to the next section. We have shown that the R line is dependent upon the barometric pressure, saturation of the gas with water, and the temperature at which saturation is achieved. The R line, thus derived, describes all possible combinations of Po_2 and Pco_2 that can exist in the gas phase of an oxygenator which contains only O_2, CO_2, and H_2O in the oxygenating mixture. The difference between the P_I and P_C points on the R line is determined by the ratio of the rate of gas flow through the oxygenator to the rate of the CO_2 production, and since in the disc oxygenator there is no dead space, $P_C = P_E$.

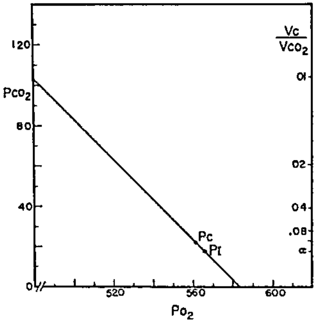

Fig 5

III. FACTORS DETERMINING THE PO_2 AND PCO_2 OF THE ARTERIAL BLOOD

If the oxygenating system is efficient enough to establish equilibrium between the gas phase and the blood phase, as is essentially the case in human lungs, the arterial tensions of O_2 and CO_2 will be identical with those of the chamber gas To the extent that the oxygenator is not 100 per cent efficient, the arterial point will differ from point *C* on the $Po_2 = Pco_2$ diagram. This difference, however, will conform to a definite ratio of Pco_2 to Po_2.

Comroe[2] states that the ratio of the diffusion of CO_2 to O_2 is defined by:

$$\frac{Do_2}{Dco_2} = \frac{Sol._{O_2}}{Sol_{CO_2}} \sqrt{\frac{M.W._{CO_2}}{M.W._{O_2}}}.$$

At 37° C., the gas phase–blood phase gradient will be approximately 20 times as great for O_2 as for CO_2. Fig. 6 expresses this relationship graphically. On this graph we have returned to the original scale on the $Po_2 - Pco_2$ diagram. If, by means described in a previous section, the chamber tensions of the gases in the gas phase are held so that Pc_{CO_2} is 17 mm. Hg, the middle Pc point on the graph, one can draw a line from that point toward the Pco_2 axis with a slope of –1/20. This line describes all possible arterial blood tensions of O_2 and CO_2 that could exist with this Pc point. Three such lines are indicated on the graph. Note that the lines are parallel and that their intercept with the R line is determined by the Pc. These lines are called $O_2 - CO_2$ diffusion ratio lines ($\dot{D}o_2/\dot{D}co_2$). It should be emphasized that the diffusion ratio lines have a slope of –1/20 only at 37° C., since a change of temperature does not affect the solubilities of the two gases proportionately. If the operating temperature is less than 37° the slope becomes smaller—at 15° C. it is approximately –1/25.

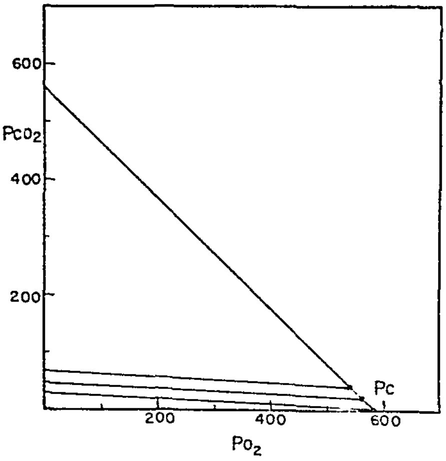

Fig. 6.

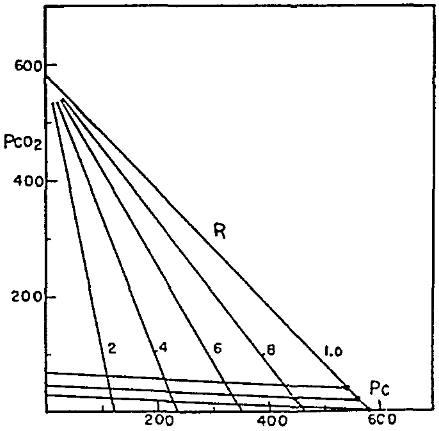

Fig. 7.

Now we must take up the question of the factors that define the position of the PA point on its diffusion ratio line. Earlier it was stated that if any oxygenator is completely efficient, that is, if there is complete equilibration between the gas phase and the blood phase, the chamber gas point will be identical with the arterial blood point. If this argument is carried further, we can define the position of the arterial blood point in terms of the efficiency of the oxygenator. The efficiency of oxygenators can be defined in many ways. For present purposes, let us make the arbitrary definition that the equilibrating efficiency of an oxygenator is the fraction that Pa_{O_2} is of Pc_{O_2}. For example, if the Pc_{O_2} is 560 mm. Hg, and the Pa_{O_2} is 100 mm. Hg, the equilibrating efficiency of the oxygenator at that time is 100 divided by 560 or 0.179. Fig. 7 graphically expresses the equilibrating efficiency lines as radiating from the intercept of the R line on the Pco_2 axis. The reader will note that the fractional efficiency of 1.0 coincides with the R line. The diffusion ratio lines are given for Fc_{CO_2} of 0.00, 0.03, and 0.06. The intercept of the diffusion ratio lines with the efficiency lines defines the tensions of CO_2 and O_2 of the arterial blood.

The equilibrating efficiencies of oxygenators vary from type to type. Indeed, the equilibrating efficiency of a given oxygenator may vary from moment to moment depending on the conditions of the perfusion. In simplest terms, however, the equilibrating efficiency of any oxygenating system is a function of the time during which a given surface area of blood is exposed to the chamber gas. Thus, for all types of oxygenators the equilibrating efficiency is a partial function of the time required for the blood to flow through the oxygenating system. Obviously, if blood is flowing through an oxygenator very slowly a higher efficiency will be achieved. Other factors are peculiar to the type of oxygenator being used. For example, the equilibrating efficiency of the rotating disc oxygenator is varied by the size, shape, and number of discs as well as by the revolutions per minute of the discs and the turnover rate of the blood in the oxygenator. During any given perfusion, however, the equilibrating efficiency is determined primarily by the ratio of disc speed to blood flow rate assuming the $P\bar{v}_{O_2}$ is kept constant. As the disc speed increases, the equilibrating efficiency increases; as the blood flow rate increases, the equilibrating efficiency decreases. The consequences of these relations will be mentioned after a description of the next graph.

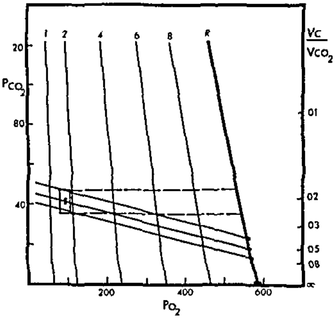

Fig 8

To combine the graphs relating the control of Pc and the control of Pa, we need to change the P_{CO_2} scale slightly as in Fig 8. The P_{O_2} axis is the same as that shown previously. The P_{CO_2} axis has been expanded so that its narrower biologically permissible limits can be observed more closely. Changing this axis makes the R line and the efficiency lines appear more vertical; their geometric slopes, however, are the same as shown on the previous graph. The same statements apply to the $\frac{D_{O_2}}{D_{CO}}$ lines. The right hand ordinate has a V_C/V_{CO_2} scale appropriately adjusted to the P_{CO_2} axis. The PI point indicates that 100 per cent O_2 is the influent gas. The small rectangle in the left portion of Fig 8 is the area of normal values. This area encompasses the range of values which occur in normal humans, as reported in the *Handbook of Biological Data*[8]

Horizontal projections, from this rectangle, to the R line encloses an area which, for the sake of discussion, shall be referred to as the permissible area. The permissible area includes values of Pa_{O_2} and Pa_{CO_2} which can conservatively be stated to be safe for several hours.

The relationships defined by the graph of Fig. 8 reveal a number of interesting points. In order to maintain normal arterial tensions of the respiratory gases, the oxygenator must have a low equilibrating efficiency—between approximately 0.15 and 0.19. The O_2 to CO_2 diffusion ratio lines, which pass through the normal area, intercept the R line between 14 and 24 Pc_{CO_2}. This means that the CO_2 tensions in the effluent gas must be maintained between 14 and 24 mm. Hg, and the equilibrating efficiency must be kept between 0.15 and 0.19 if the arterial respiratory gas tensions are to be maintained in the normal area. These PE_{CO_2} values correspond to 2.5 and 4.1 per cent CO_2 when the oxygenator is operated under the conditions assumed. The graph also shows that to maintain this PE_{CO_2} or Pc_{CO_2} the ratio of the rate of gas flow to the rate of CO_2 production must be maintained between 0.06 and 0.036 if the oxygenating gas is 100 per cent O_2.

Another interesting point that the graph reveals might be worth mentioning. A change in efficiency results in a much larger change in the Pa_{O_2} than in the Pa_{CO_2}. Conversely, a change in Pc_{CO_2} has a greater effect on the Pa_{CO_2} than on the Pa_{O_2}. These facts enable the perfusionist to dissociate control of Pa_{O_2} and Pa_{CO_2} to a large extent. In the disc oxygenator, the efficiency, and, therefore, the PA_{O_2} can be controlled by the perfusionist's control of the disc speed—pump rate ratio. In the bubble oxygenator, the same can be accomplished by a variation in bubble size—the larger the bubbles the smaller the oxygenating efficiency. The Pc_{CO_2} and, therefore, the Pa_{CO_2} can be controlled by the perfusionist's alteration of the ratio of the rate of gas flow to the rate of CO_2 production, or by a change in the per cent of CO_2 in the influent gas. Either type of control can be used by the perfusionist. However, it is probably simpler to vary the rate of flow of oxygen, since this avoids the necessity of having two tanks of oxygenating gas with different fractions of CO_2, and of having mixing gauges which are accurate.

IV. FACTORS DETERMINING THE PO_2 AND PCO_2 OF THE VENOUS BLOOD

Now we must consider the interrelations of those factors which define the difference between the tensions of the respiratory gases in the arterial blood and in the venous blood, i.e., the difference between the Pa point and the $P\overline{v}$ points on the $PO_2 - PCO_2$ diagram. Instead of going directly to the $PO_2 - PCO_2$ diagram, however, we shall take a few intermediate steps of gentler intellectual grade. We shall first describe how a living organism solves this problem, and then we shall see how the artificial pump-oxygenator can be operated to mimic this solution.

One of the simplest approaches is via the Fick equation which states:

$$\dot{V}O_2 = \frac{\dot{Q}B\ (Ca_{O_2} - C\overline{v}_{O_2})}{100} \tag{6}$$

or that the total oxygen consumption of the body is equal to the cardiac output times the arterial-venous oxygen difference. This relationship can be graphically expressed as shown in Fig. 9. The ordinate of this graph is the rate of oxygen consumption, and the abscissa is the cardiac output. The lines radiating from the origin are the arterial-venous oxygen differences. Therefore, the slope of the relationship between the oxygen consumption and cardiac output is defined by the arterial-venous oxygen difference. The dots represent data obtained from a series of normal humans studied at this institution.[7] From this graph, one would conclude that variations in oxygen consumption amongst individuals are met by variations in cardiac output sufficient to maintain a normal $Ca_{O_2} - C\bar{v}_{O_2}$. It would seem, therefore, that one of the ideals of perfusion would be to deliver the rate of blood flow which meets the oxygen consumption demands and maintains an arterial-venous oxygen difference between 5.5 and 3.5 vol. per cent. However, it would seem reasonable that circumstances could occur in which this ideal is achieved and yet have the organism in severe difficulty by not taking proper account of Co_2 transport. In order to include a consideration of CO_2, let us make another approach by means of the Co_2 – Cco_2 diagram. Such a diagram can relate the contents of O_2 and CO_2 in the blood through the following equation,

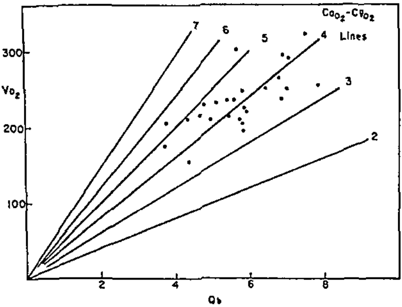

Fig 9.

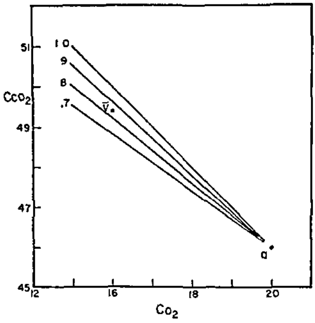

Fig. 10.

$$R_B = \frac{C\bar{v}_{CO_2} - Ca_{CO_2}}{Ca_{O_2} - C\bar{v}_{O_2}} \qquad (7)$$

and in a steady state:

$$R_B = R.Q. \qquad (8)$$

The ordinate of Fig. 10 is the Cco_2 and the abscissa is the Co_2.

The units for each coordinate are volumes per cent. If an individual has Ca_{CO_2} of 20 and Ca_{O_2} of 46, this can be graphed as point *a* on Fig. 10. The lines radiating from *a* are the R_B lines or the blood respiratory exchange ratio lines. When the individual is in a steady state, R_B is equal to R.Q., and the

R.Q., then, defines the RB line on which the $\bar{v}$ point must lie. The hypothetical points plotted are for an individual with Ca_{O_2} of 20, Ca_{CO_2} of 46, $C\bar{v}_{O_2}$ of 16, $C\bar{v}_{O_2}$ of 49, and R.Q. of 0.85.

One problem with this diagram is its failure to relate the factors which define where the $\bar{v}$ point will fall on its RB line. A slight addition to the graph, however, allows this to be done. The $Ca_{O_2} - C\bar{v}_{CO_2}$ can be estimated from Fig. 10 by simply determining the differences between the *a* point and $\bar{v}$ point on the graph. Then let us rearrange (6) to,

$$\frac{\dot{V}O_2}{Q_B} = \frac{Ca_{O_2} - C\bar{v}_{O_2}}{100} \tag{9}$$

and by the same reasoning we get,

$$\frac{\dot{V}CO_2}{Q_B} = \frac{C\bar{v}_{CO_2} - Ca_{CO_2}}{100} \tag{10}$$

Equations (9) and (10) can be added to (7) and (8) to obtain,

$$R.Q. = R_B = \frac{C\bar{v}_{CO_2} - Ca_{CO_2}}{Ca_{O_2} - C\bar{v}_{O_2}} = \frac{\dfrac{\dot{V}CO_2}{Q_B}}{\dfrac{\dot{V}O_2}{Q_B}} \tag{11}$$

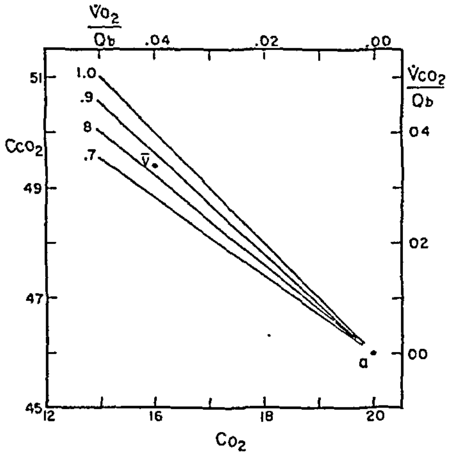

Fig. 11.

These relations can be added to Fig. 10 to obtain Fig. 11. The right ordinate and upper abscissa are the $\frac{\dot{V}CO_2}{Q_B}$ and the $\frac{\dot{V}O_2}{Q_B}$, respectively. This graph shows that the difference between the *a* point and the $\bar{v}$ point on the RB line is determined by the ratio of the rate of O_2 consumption to the cardiac output or the ratio of the rate of CO_2 production to the cardiac output. *We see again that the body adjusts the cardiac output to the metabolic needs of the individual. The same feat could be accomplished by the pump-oxygenator if the contents of the respiratory gases in blood could be continuously monitored. This would allow the perfusionist to adjust the rate of blood flow to the metabolic needs of the patient without knowing either. Unfortunately, however, such instrumentation is not presently available; therefore, another solution must be sought.*

Currently, pH, Pa_{O_2} and $P\bar{V}_{O_2}$ can be monitored Is it possible to derive a graph in these terms which would guide the perfusionist in achieving this adjustment of blood flow to metabolic needs? The next several graphs are steps in this derivation

The relationships expressed in Fig 11 on the Co – Cco diagram can also be expressed on the Po_2 – Pco diagram The form is not as convenient, because the dissociation of oxyhemoglobin is not linear Let us recall the familiar oxyhemoglobin dissociation curve to mind and see how it can be expressed in a form that is more useful for present purposes Fig 12 shows the relationships amongst Po , Pco_2, and Co_2 in human blood at 37° C It is of importance to mention, at this point, the known and unknown effects of hypothermia on these curves It is well established that cold shifts the dissociation curve, of a given Pco_2, to the left It is not clear from the literature what the Pco_2 has to be increased to in order to shift the curve back to the right This important group of facts is not presently available to those who combine hypothermia and extracorporeal circulation This is the subject of a current investigation in this laboratory Now let us project a line horizontally from the Co_2 axis at 15 vols per cent The projected line is a line of constant Co_2 Note that it crosses each of the dissociation curves These points can be plotted as tensions on the

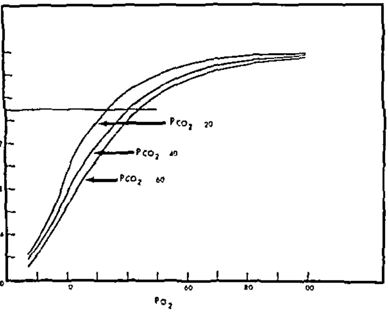

Fig 12

Po_2 – Pco_2 diagram and the points joined by a smooth curve, the constant oxygen content curve Such dissociation curves are shown on the Po – Pco_2 diagram of Fig 13 for a Co of 6, 10, 14, 15, and other values The volumes per cent of each line is expressed at the top of the line Now if any two of the three relationships mentioned above are known, a point representing Pa can be plotted which simultaneously shows the magnitude of Pa_{O_2}, Pa_{CO_2}, and Ca_O Let "a" be the arterial point of a hypothetical individual You will recall from Fig 11 that the venous point is partially defined under these conditions by the ratio of the oxygen consumption of the individual to his cardiac ouput You will recall further that this ratio is equal to the A V oxygen difference (Ca_{O_2} – $C\bar{V}_{O_2}$) The $\frac{\dot{V}_{O_2}}{Q_B}$ is indicated on Fig 13 below the lines of equal oxygen content, whatever line "a" falls on will have infinity as the value of this ratio. If the $Ca_{O_2} - C\bar{v}_{O_2}$ of the individual is in the normal range (3.5-5.5 vols, per cent) the $\frac{\dot{V}O_2}{\dot{Q}_B}$ must be between 0.0355 and 0.055 as seen in Fig. 9, and the venous point must lie somewhere between these lines. Where the venous point will lie with respect to the P_{CO_2} axis can be predicted from a knowledge of the C_{CO_2} of the blood.

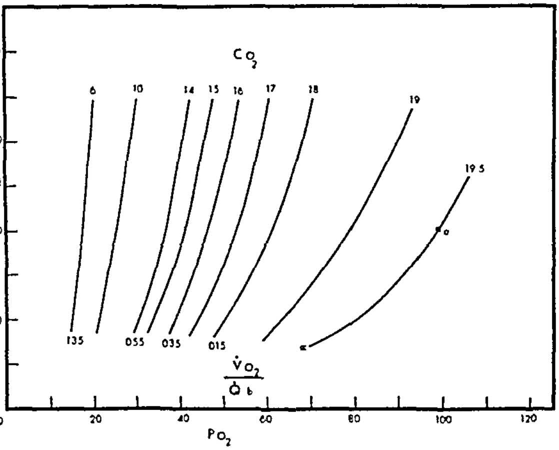

Fig. 13.

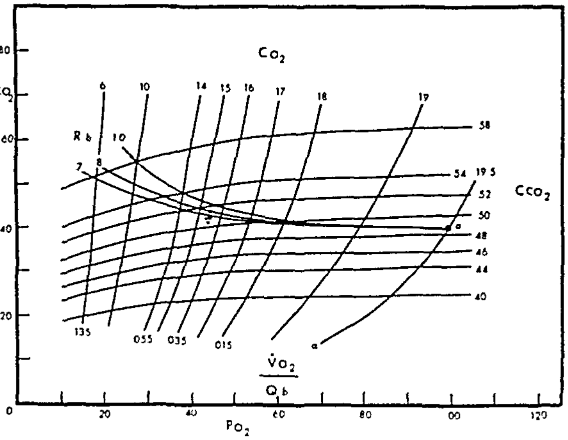

Fig. 14.

Let us relate the CO_2 content of the blood to the $P_{O_2} - P_{CO_2}$ diagram. This can be done, for blood with an oxygen capacity of 20 volumes per cent, by utilizing the quantitative relations of the Bohr effect as contained in the nomogram of Dill and his associates.[3] Fig. 14 is similar to Fig. 13 with certain additions. The lines coming up from the lower left-hand corner and extending horizontally almost parallel to the P_{O_2} axis are lines of equal CO_2 content of blood. With this addition it is now possible to draw in the R_B lines as was done on Fig. 11. The curved lines radiating from *a* are the R_B lines ranging from 1.0 to 0.7. It will be recalled that in a steady state the R_B lines are equal to the R.Q. of the individual.

The venous point described on the graph of Fig. 14 is therefore that in an individual with an R.Q. of 0.8 and a normal A-V oxygen difference of 4 vols. per cent. This individual then would have a C_{CO_2} of 51.5 vols. per cent, $P\bar{v}_{CO_2}$ of 44, and a $P\bar{v}_{O_2}$ of 44.

One interesting fact revealed by this graph is that if the arterial point is controlled along the P_{CO_2} and the P_{O_2} axes, the venous point would have to be controlled only along the P_{CO_2} axis, since large changes in R.Q. cause only small changes in $P\bar{v}_{CO_2}$. The control of the venous point along the P_{CO_2} axis is dependent on the ratio between the rate with which oxygen of the blood is being removed by the tissues to the CO_2 being added to the blood from the tissues or the Rb. As mentioned earlier, however, at the present time we lack instrumentation to define adequately the arterial point along the P_{CO_2} axis. And, another difficulty with this form of graph is that CO_2 content, which allows one to depict the Rb lines, is referable only to an individual with the specific oxygen capacity of the blood of 20 vols. per cent.

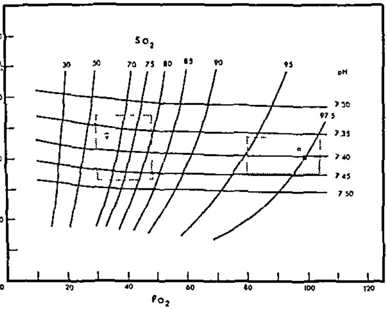

Fig 15.

The relations depicted in Fig. 14 can be generalized and made more useful for the adaptation of the artificial pump-oxygenator *by changing the lines of equal oxygen content to lines of constant oxyhemaglobin saturation.* In addition, *the lines of constant carbon dioxide content can be changed to become lines of constant blood pH.* These relations are illustrated in Fig. 15 and allow us to fix the arterial point on the X axis by monitoring either the P_{O_2} or the per cent saturation of blood. The arterial point can be fixed with reference to the Y axis by continuous monitoring of the P_{CO_2} or the pH. The venous point can be fixed on the X axis by monitoring either the P_{O_2} or per cent saturation of the venous blood; and as we saw in the previous graph, it is unnecessary to fix the venous point on the Y axis. However, if such information were desired, this point could be fixed by monitoring either the venous pH or the venous P_{O_2}. Since instrumentation is currently under development for each of the four parameters related on Fig. 15, this graph becomes a most useful one in describing a physiologic perfusion. The choice of the two parameters to be monitored is left to the experience of the perfusionist.

An interesting point might be made in reference to the accuracy with which one must measure these parameters in order to perform as well as the body. The rectangles enclosed by dotted lines describe the normal values for Pco_2 and Po_2 that are listed in the *Handbook of Biological Data.*[8] The range of normal Pa_{O_2} is from 80 to 104 mm. Hg. If one recalls that the permissible range of Pa_{O_2} includes much higher tensions, it becomes apparent that if one chooses to monitor the Pa_{O_2} and maintain it at 100, he needs only to measure this parameter with an accuracy of plus or minus 20 per cent in order to maintain this value within acceptable limits. If one chooses to monitor the arterial point on the X axis by means of per cent saturation, it is apparent that no such gross instrumental error can be allowed. Similarly, the normal range of Pa_{CO_2} is from 45 to 47. Therefore, if one choses to fix the arterial point with respect to the Y axis by monitoring the Pa_{CO_2}, instrumentation that was accurate within plus or minus 15 per cent would do as well as the body. If he chooses to fix this point by monitoring pH, instrumentation that will have an accuracy of plus or minus 0.05 pH units is required. The normal range of $P\bar{v}_{O_2}$ is 30 to 48 mm. Hg. Again, if one chooses to monitor this point by means of Po_2 measurements, the accuracy required is not great—plus or minus 20 per cent will keep the venous point well within these limits. If one is using the venous saturation, more latitude is allowed for error here than in the arterial point. Finally, there is no need to fix the venous point with reference to the Y axis as was indicated by the relations drawn in the previous diagram.

V. ONE POSSIBLE ADAPTATION OF THESE STUDIES WHICH ADEQUATELY CONTROLS WHOLE BODY PERFUSION

Fig. 16 includes the key points of the previous graphs expressed in physiologic terms which would theoretically allow one to monitor adequately and control the arterial and venous points and to make appropriate adjustment to their change. Fig. 17 is the same graph expressed in terms of functions of the pump-oxygenator. The arterial point lies on the straight dotted line which is the $O_2 - CO_2$ diffusion ratio line. This line and, therefore, point *a* on the line moves in the upward direction with an increase in CO_2 production by the patient being perfused. The upward movement of *a* is impeded by an increase in the rate of flow of gas through the oxygenator. The slope of the line along which *a* moves up and down is that of an equilibrating efficiency of 0.18. Moreover, *a* can move along the $O_2 - CO_2$ diffusion ratio line by a variation in the efficiency. This efficiency during a perfusion with the disc oxygenator would allow *a* to be moved to the right by an increase in disc speed and it would move to the left when there was an increase in the rate of perfusion of the patient. If the device for measuring the Pa_{O_2} has an accuracy of ±20 per cent, the perfusionist can adjust the disc speed of the oxygenator so that the apparent Pa_{O_2} is 100 mm. Hg and know that the true Pa_{O_2} lies within the permissible range. The perfusionist would not vary the rate of blood flow by the pump in order to change the *a* point. As shall be seen later, the perfusionist is committed to deliver a rate of blood flow to the patient that maintains a normal $P\bar{v}_{O_2}$. If the perfusionist has a device that will continuously measure arterial blood pH to within ±0.05 pH units, he can vary the rate of flow of oxygen through the oxygenator so that the apparent arterial pH is 7.40 and be assured that the arterial pH and P_{CO_2} are within the normal limits. With the arterial point fixed in this manner, the perfusionist knows that the venous point lies somewhere along the RB line that the patient is on at that particular time. The RB line indicated on Fig. 16 is that of 0.8, a reasonable fasting value.

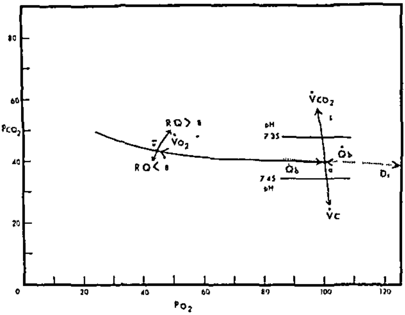

Fig 16

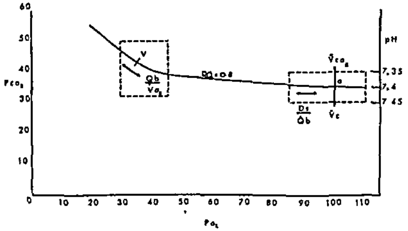

Fig 17

The perfusionist need only fix the venous point with respect to the oxygen tension. If the device with which the perfusionist is monitoring the $P\bar{v}_{O_2}$ is accurate within ±20 per cent, the pump flow rate can be adjusted so that the apparent $P\bar{v}_{O_2}$ is 40 mm. Hg and the true $P\bar{v}_{O_2}$ will lie well within the normal range for this parameter. If the oxygen consumption of the patient is higher than anticipated the venous point will move to the left along the RB line. To compensate for this effect the perfusionist must increase the blood flow rate from the pump. Conversely, if the perfusion rate is too high the venous point will move to the right along the RB line, and the rate of perfusion should be decreased.

To illustrate more fully how this system is linked together it might be of value to relate what might happen in a hypothetical case. Let us assume that we have estimated the oxygen consumption of the individual to be perfused, from some body weight-height nomogram. From this information and Fig. 9 one can estimate the rate of blood flow that might be required for this patient. If hypothermia is used, a lower value would obtain. From this data one could also, by assuming an R.Q. of 0.8, estimate the rate of CO_2 production that such an individual might have. From this estimated rate of CO_2 production and knowledge that a gas flow rate to CO_2 production rate ratio of 0.05 is desirable, one could calculate what rate of flow of gas might be required for this patient in order to maintain a normal arterial pH. From empirical data relating the rate of blood flow to disc speed that is appropriate to give an oxygenating efficiency of 0.18, the perfusionist would then have an estimate of the disc speed that might be required by this patient. Let us assume that the perfusionist begins to perfuse the patient with these first estimates, and he finds that the $P\bar{v}_{O_2}$ is 30 mm. Hg. This means that he has underestimated the rate of oxygen consumption of the individual and he must increase the rate of blood flow to the patient. As he increases the rate of blood flow to the patient to bring the venous point to a higher Po_2 level, this causes the arterial point to move to the left. The Pa_{O_2} will decrease because the equilibrating efficiency will have decreased by the increase in blood flow to the patient. This fact then demands that the perfusionist increase the disc speed so that the apparent Pa_{O_2} is 100 mm. Hg. Since the initial estimate of the rate of oxygen consumption of the patient was low, it is probable that the estimate of the rate of CO_2 production was also low. If this is true, then the arterial point would initially move up on the graph as it moved to the left. The perfusionist then would increase the rate of oxygen flow through the oxygenator to return the pH to 7.40.

SUMMARY

The cardiorespiratory characteristics of artificial pump-oxygenating systems have been theoretically analyzed by the use of graphical analysis. To make this analysis as simple as possible, several simplifying assumptions were made. This analysis described several combinations of monitoring systems that might be used to give the patient an adequate perfusion without exact knowledge of either the rate of oxygen consumption of the patient or of the perfusion rate. One of these possible systems was described in some detail for use with a rotating disc oxygenator. This system is in current use at the University of Colorado Medical Center. How close real perfusions come to the ideals described in the present paper will be the subject of a future report.

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PULMONARY VENTILATION IN HYPOTHERMIA

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As compared with investigation of cardiovascular changes during hypothermia, relatively little work has been done on the ventilatory system. Breathing is generally described in terms of two components: (1) ventilation and (2) respiration.[1] Ventilation constitutes the mass movement of air in and out of the lungs and the distribution of air within the alveoli. This activity is achieved through the mechanical parts of the breathing apparatus, measurements of which include lung volumes, maximum breathing capacity, minute ventilation, and intrapulmonary gas distribution. Respiration is the physicochemical phase which involves the transport of gases by the blood and their exchange across the alveolocapillary membrane. To the latter, a fundamental component is the pulmonary capillary blood flow.

Studies on respiration changes in hypothermia have demonstrated a respiratory acidosis.[2, 5, 9] Diffusion of gases across the alveolocapillary membrane is apparently not adversely affected.[6] Oxygen consumption decreases linearly with falling temperature.[8] Severinghaus and Stupfel[7] found that the compliance was somewhat decreased and the dead space increased. Death from hypothermia is generally attributed to respiratory failure followed by circulatory failure.[5]

The retention of CO^2, as evidenced by the respiratory acidosis in hypothermia, may be due to deficient ventilation. The present study is an evaluation of the effect of hypothermia upon some aspects of the mechanical component of ventilation as assessed by minute ventilation, helium excretion as an index of intrapulmonary gas distribution, and the functional residual capacity (FRC).

METHOD AND MATERIAL

Study was carried out on dogs under chloralose anesthesia and with unassisted ventilation. Despite the fact that, in heavy doses, chloralose can produce central respiratory depression, respiratory reflex excitability under this agent is increased.[3] Following the achievement of a relative "steady state," as determined by rate and depth of respiration, the functional residual capacity and rate of excretion were determined by the open-circuit helium method.[4]

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Essentially, in this method, the animal breathes a 50-50 mixture of helium and oxygen for a period of 10 minutes to allow for equilibration of the gas in the alveoli. At the end of a normal expiration, the animal is switched to tank oxygen and the helium is washed out. The helium is passed through a system for continuous analysis by a sensitive katharometer.* The rate of excretion of of helium serves as a general index of the gas mixing. The gas is collected in a Douglas bag from which the minute ventilation and the functional residual capacity is calculated. All gases have been corrected to STPD (standard temperature pressure dry).

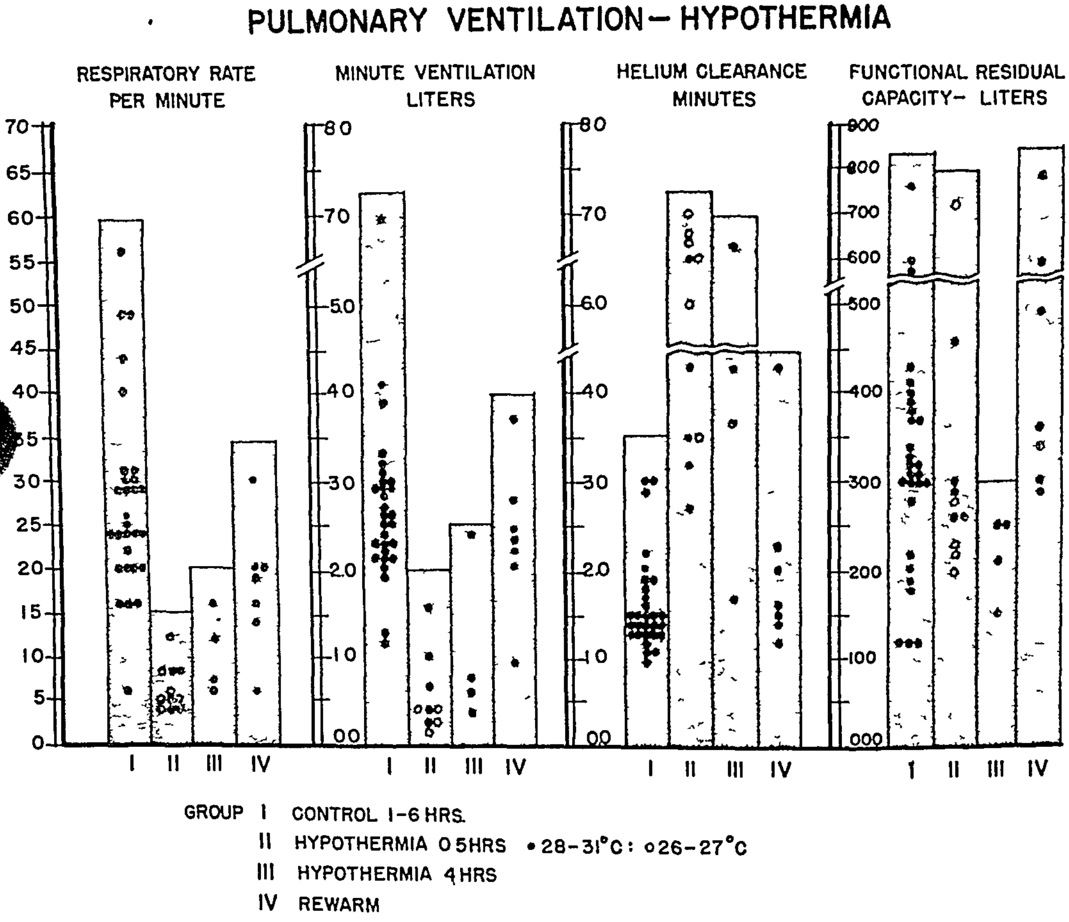

Fig 1.—Significant depression in pulmonary ventilation occurs only below 28° C In prolonged hypothermia (4 hours) there is improvement in over-all ventilation. Upon rewarming ventilation returns toward normal

Animals in the study were divided into the following groups: *Group A*—Control. Six animals under chloralose anesthesia with analyses at 1, 3, and 6 hours of anesthesia to determine the effects of this agent over a prolonged period of time. *Group B*—Seven animals subjected to hypothermia ranging from 31° to 27° C., and then rewarmed. *Group C*—Four animals cooled to levels of 27° to 26° C. and maintained for 4 hours at this temperature.

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*Gow-Mac Instrument Co, Madison, New Jersey

TABLE I. PULMONARY VENTILATION—NORMOTHERMIA CONTROLS
AVERAGE OF 6 DOGS—CHLORALOSE ANESTHESIA

TIME (HOURS)	RATE PER MIN	MINUTE VENTILATION (L./MIN.)	TIDAL VOLUME (ML.)	HELIUM CLEARANCE (MIN.)	FUNCTIONAL RESIDUAL CAPACITY (ML.)
1	29	2.44	110	1.8	310
3	30	2.90	95	1.5	440
6	32	3.70	110	1.5	370

RESULTS

Group A.—Controls. The averages of the 6 animals are compiled in Table I. Over a period of 6 hours there was no significant change in the respiratory rate. Seventy per cent of the animals had a rate between 20 and 30 per minute, as shown in Fig. 1. The minute ventilation increased during the latter part of the study. For the entire group, 83 per cent of the animals had a minute ventilation between 2 and 3 L. The tidal volume remained essentially unchanged, and averaged 100 ml. The clearance of helium was essentially unchanged, and, in 90 per cent of the animals, this time varied from 1 to 2 minutes with an over all average of 1.5 minutes. The functional residual capacity was quite variable in this group, with 59 per cent having an FRC of 300 to 400 ml. Except for a significant increase in the minute ventilation and a minimal increase in the FRC, there were no gross changes in ventilation during the 6 hour period of control anesthesia observation.

TABLE II. GROUP B. HYPOTHERMIA AND REWARM—CHLORALOSE ANESTHESIA

NO.	TEMPERATURE (°C.)	RATE PER MIN.	MINUTE VENTILATION (L./MIN.)	TIDAL VOLUME (ML.)	HELIUM CLEARANCE (MIN.)	FUNCTIONAL RESIDUAL CAPACITY (ML.)
1	39.2	20	2.89	145	1.9	395
	31.0	12	1.56	130	2.7	455
	39.2*	16	2.33	145	2.3	490
2	38.6	16	1.21	76	3.0	310
	31.0	8	1.00	125	3.2	300
	39.3*	30	2.22	74	1.4	300
3	38.0	24	2.63	109	2.0	200
	30.0	8	0.66	82	3.5	260
	37.4*	14	3.69	265	1.2	290
4	39.2	20	2.58	130	1.5	330
	28.1	4	0.25	63	6.5	260
	39.2*	20	2.79	140	1.5	780
5	38.2	24	2.25	94	1.5	119
	27.8	5	0.38	77	4.3	290
	38.5*	18	2.05	115	2.0	590
6	39.2	20	2.10	105	1.5	370
	27.2	4	0.24	60	6.0	220
	39.2*	20	2.35	120	1.6	340
7	37.5	16	2.47	155	1.5	120
	27.2	4	0.36	90	6.5	280
	37.5*	6	0.96	160	4.3	360

*Rewarm

Group B.—Data referable to the animals cooled and then rewarmed appear in Table II. There was significant reduction both in the respiratory rate and in the minute ventilation at all levels of hypothermia studied (31°-27°). However, marked prolongation of time required for helium clearance occurred only at 28° C. and below. Generally, the deeper the hypothermia, the greater the decrease in minute ventilation and the greater the increase in time required for helium clearance. The FRC during hypothermia did not show any significant alteration for the hypothermic group as a whole. Upon rewarming, the respiratory rate returned toward normal. The minute ventilation increased and, in the majority of animals, fell within the normal range. The helium clearance time returned to essentially normal limits. The FRC remained somewhat high in less than half the animals rewarmed.

Group C.—Following 4 hours of hypothermia, the animals demonstrated improvement in their ventilation. The respiratory rate increased somewhat as shown in Table III. The minute ventilation and tidal volume improved, and the time required for helium clearance in 3 of the 4 animals was reduced. The FRC also became somewhat reduced as compared to the short-term hypothermic group (Fig. 1).

TABLE III. GROUP C. PROLONGED HYPOTHERMIA (4 HOURS) AND CHLORALOSE

NO.	TEMPERATURE (°C.)	RESPIRATORY RATE PER MIN.	MINUTE VENTILATION (L./MIN.)	TIDAL VOLUME (ML.)	HELIUM CLEARANCE (MIN.)	FUNCTIONAL RESIDUAL CAPACITY (ML.)
1.	37.3	48	2.94	61	1.1	120
	26.2	8	0.40	50	3.5	230
	26.5*	16	2.42	150	1.7	210
2.	37.6	16	2.41	150	1.1	280
	26.0	4	0.19	48	6.8	200
	27.0*	7	0.57	80	3.7	250
3.	37.9	24	2.00	83	2.8	340
	27.0	5	—	18	—	720
	27.0*	6	0.36	60	6.7	250
4.	38.2	22	2.14	97	1.3	310
	27.4	5	—	—	8.7	—
	26.4*	12	0.73	61	4.3	150

*Hypothermia – 4 hours.

DISCUSSION

Hypothermia results in a marked reduction in pulmonary ventilation, as evidenced by reduced respiratory rate and minute ventilation. This has been observed by other investigators.[2, 8] Helium clearance which provides a general index of intrapulmonary gas mixing was prolonged suggesting impairment of ventilation. The depressed ventilation appears to be essentially a function of the reduced temperature. As shown in Fig. 2 there is a linear relationship between the respiratory rate and the minute ventilation. As the rate becomes significantly reduced, the minute ventilation concomitantly becomes smaller. If mechanical components concerned with ventilation were unaltered by hypothermia, it might be anticipated that, despite the reduced rate, the volume of air moved in and out of the lungs might be fairly considerable; however, in these studies this is apparently not the case, suggesting some impairment in the mechanics of breathing. The defective alveolar ventilation during hypothermia is demonstrated in Fig. 3. There is, in general, a parabolic relationship between minute ventilation and the excretion of helium. Below a ventilation rate of 1 L. per minute, the time required for excretion of helium may vary from 3 to 7 minutes. Of significance, however, is the fact that this activity returns to normal upon rewarming. A ratio between minute ventilation (MV) and the helium excretion time (He_t), termed the ventilation efficiency ratio (VER), was developed to illustrate the changes of efficiency of ventilation during hypothermia. A VER not exceeding 0.4 is considered to be within normal limits. As demonstrated in Fig. 4, the efficiency becomes very markedly reduced at hypothermic levels of 28° C. and below with, however, significant improvement in ventilatory efficiency at the end of 4 hours of cold exposure. The improvement of ventilation during prolonged hypothermia is doubtless due to an improvement in over-all ventilation. This might well be due to a response of the respiratory center to the pCO_2 stimulus since, during hypothermia, the pCO_2 becomes elevated.[1] While there is a possibility that the reflex responses to CO_2 may be depressed, it appears likely from this study that, while thresholds to stimuli may alter somewhat, elevated pCO_2 may still elicit an adequate response from peripheral respiratory reflexes in prolonged hypothermia.

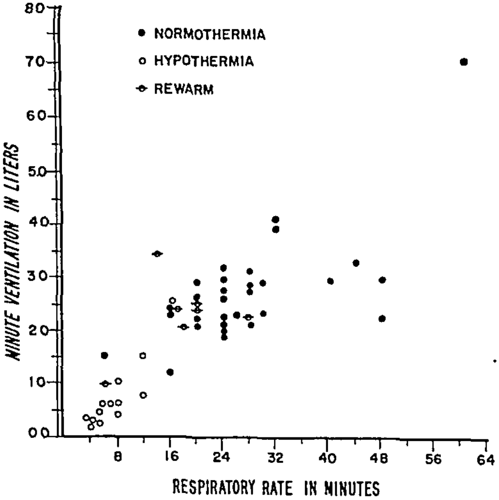

Fig. 2.—A generally linear relationship between respiratory rate and minute ventilation is demonstrated. The relationship is retained during hypothermia, suggesting mechanical as well as central and/or reflex depression

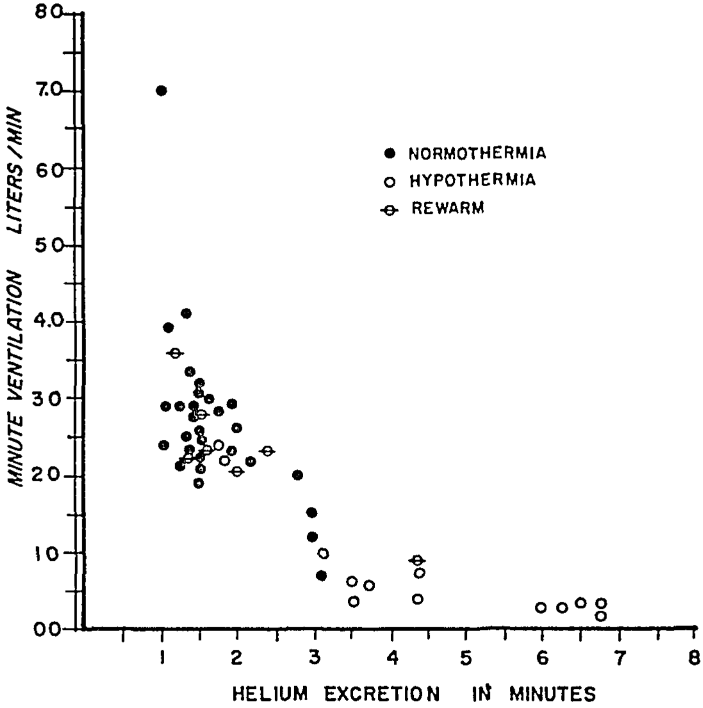

Fig. 3.—Depression of the minute ventilation during hypothermia is accompanied by increased defective in rapulmonary gas mixing, as indicated by prolonged excretion time of the helium. The degree of defective gas distribution varies greatly. These functions return to normal on rewarming.

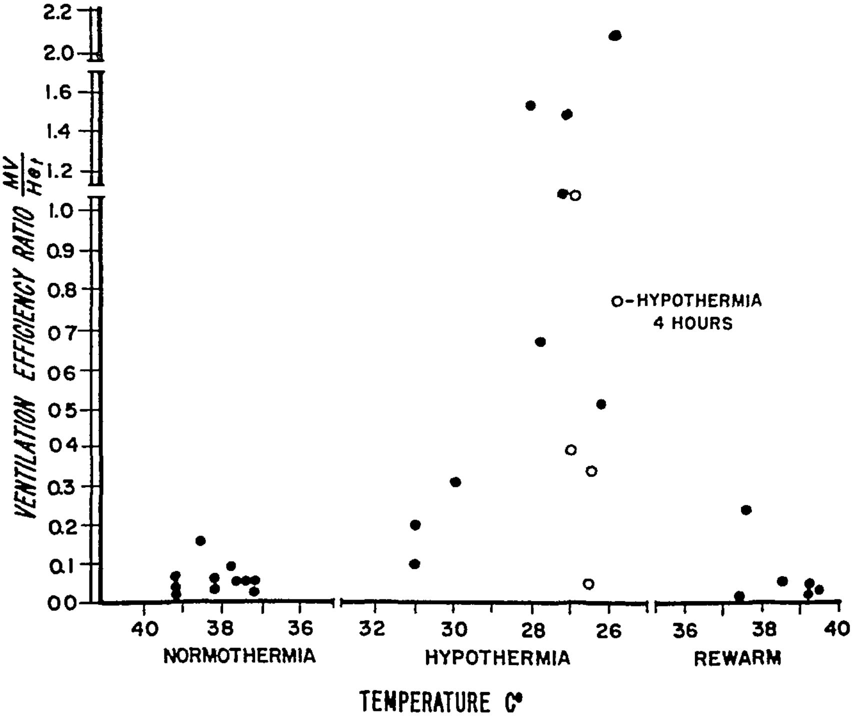

Fig. 4.—The efficiency of ventilation is seriously reduced at 28° C. and below, with improvement during prolonged hypothermia and return to normal on rewarming.

As a result of the marked ventilatory depression at 28° C. and lower, significant unsaturation and CO_2 retention would likely occur.

The precise involvement of the various mechanical components during hypothermia is not known. It has been demonstrated that there is some increase in dead space and some decrease in compliance.[6] These changes, along with the possible increased resistance to breathing, would indicate increased work required for breathing. Alterations in these mechanical factors, together with central depression due to cold narcosis, could well account for the reduced efficiency of ventilation as demonstrated in these studies. The changes, however, appeared to be transient, and, upon rewarming, ventilatory activity returned to normal limits.

CONCLUSIONS

Study of pulmonary ventilation was carried out in dogs under chloralose anesthesia under hypothermia and upon rewarming. The level of hypothermia varied from 31° to 26° C.

There was a marked depression in pulmonary ventilation at 28° C. and below, which improved somewhat under prolonged hypothermia. The depression is likely central in origin, although some alteration in the mechanics of breathing may also occur. The improvement after 4 hours of hypothermia is probably due to return of an adequate threshold response of the respiratory reflexes to pCO_2.

Upon rewarming, the pulmonary ventilatory functions measured returned toward normal limits.

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ACIDOSIS FOLLOWING RESPIRATORY ALKALOSIS IN THORACIC OPERATIONS WITH AND WITHOUT HEART-LUNG BYPASS

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In the past decade anesthetists have become aware of the likelihood and the danger of carbon dioxide retention during anesthesia.[3, 8] The reaction to this knowledge has been a tendency to hyperventilate the patient. With respiration thus assisted by the anesthetist, depression of the arterial carbon dioxide tension may occur, particularly with the use of a muscle relaxant and complete control of ventilation by the anesthetist. This is particularly true in children. The observations reported herein concern the blood changes that occur after respiratory alkalosis produced by prolonged hyperventilation during thoracic operations.

MATERIAL

The patients considered in this report fall into two groups—the "pump-oxygenator" group and the "control" group. The former consisted of 22 consecutive patients undergoing open heart surgery for a variety of congenital cardiac lesions using a screen-oxygenator.* There were two adults, aged 41 years and 58 years, in this group; the remainder were children weighing for the most part between 10 and 20 kilograms. Three patients died postoperatively. Two of these had had tetralogy of Fallot and the other had had a functional single ventricle with pulmonary hypertension. An anatomic cause of death was present in each case.

The control group consisted of 8 children undergoing other thoracic operations. Five had ligation of a patent ductus arteriosus, 2 had lobectomies, and 1 division of a vascular ring.

METHODS

The determinations under consideration include the arterial carbon dioxide tension (pCO_2), the whole blood pH, and the plasma bicarbonate. Measurements were made with the Astrup apparatus.[1, 2]

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The blood in all cases was warmed to 38° C, and the observations are reported for the blood at that temperature regardless of the actual blood temperature at the time of sampling Arterial samples were drawn under anaerobic conditions from a catheter in the radial artery In the pump oxygenator group, samples were drawn at the following times (1) chest open before bypass, (2) late bypass, (3) chest open after bypass, and (4) after chest closure with spontaneous ventilation In the control group, samples were drawn (1) before thoracotomy, (2) after opening the chest, (3) before closing the chest, and (4) after chest closure with spontaneous ventilation

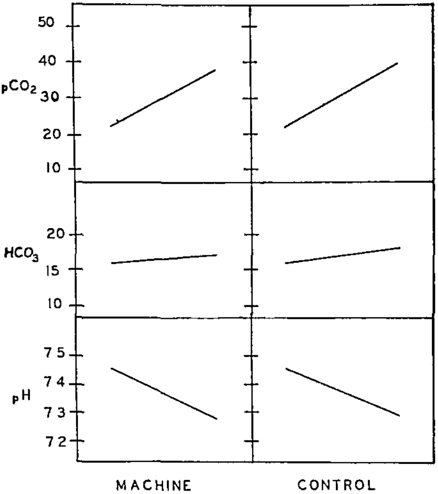

Fig 1—Arterial blood changes following prolonge mparing the heart lung bypass and the control patients In eac alues to the *left* represent conditions just prior to chest closure with anesthetist the values to the *right* indicate the situation after chest ventilation The pCO has returned to normal in each group and the

Anesthesia was similar for both groups of patients They were premedicated with pentobarbital (1 5 mg /Kg) 1½ hr preoperatively, and morphine (0 1 mg /Kg) and scopolamine (0 01 mg /Kg) 1 hr preoperatively After induction, endotracheal anesthesia was maintained with 50 per cent nitrous oxide and oxygen The patients were paralyzed with a muscle relaxant and were manually hyperventilated on a semi open system with carbon dioxide absorption

RESULTS

The results are listed in Tables I and II The carbon dioxide tension was maintained at about 22 mm Hg by the anesthetist until the patient was permitted to ventilate spontaneously When spontaneous ventilation was resumed, the average carbon dioxide tension rose from 22 to 38 and this was accompanied by a fall in pH from 7.46 to 7.29. A fall in pH always occurred. The late samples in Patient 57 have not been included in the average since there was inadequate relief of pulmonary outflow obstruction in this case of tetralogy of Fallot, and the patient had severe hypotension due to low output failure after the bypass.

TABLE I. PUMP-OXYGENATOR CASES

PATIENT NUMBER	CHEST OPEN BEFORE BYPASS			LATE BYPASS			CHEST OPEN AFTER BYPASS			AFTER CHEST CLOSURE SPONTANEOUS VENTILATION		
	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3
38	7.59	20	19.5				7.48	18	15	7.29	30	14.5
39	7.52	19	16.5				7.25	31	13.5			
40	7.50	35	26				7.48	21	16.5	7.24	42	17
41	7.42	27	18.5	7.24	50	18.5	7.33	33	17	7.20	41	15.5
42	7.54	21	18.5	7.45	25	17.5	7.43	25	16.5	7.26	51	21
43	7.56	23	21	7.44	22	15.5	7.50	20	15.5	7.32	35	17.5
44	7.40	25	15.5	7.40	19.5	13						
45	7.54	24	20.5	7.44	29	19.5	7.46	20	15.0	7.18	41.5	15.0
46				7.46	36	24.5	7.55	20	18	7.38	37	21
47				7.49	22.5	17.5	7.45	18	13			
48				7.48	22	17				7.30	42	20.5
49				7.38	29	17	7.42	22	15			
50	7.45	26	18	7.40	29	18	7.47	23	17	7.31	39	18.5
51	7.55	16.5	15.5	7.42	22	15	7.54	14.5	14	7.33	33	17
52	7.43	21.5	15	7.28	32.5	15	7.39	24.5	15	7.28	37	17
53	7.52	16	.14	7.23	40	16	7.49	18	15	7.25	35	15
54	7.58	14	14.5				7.57	16	16	7.31	33	16
55	7.55	21	18.5	7.31	35	17	7.53	18	16	7.36	30	16.5
56	7.58	21	20	7.39	35	20.5	7.44	21	15	7.25	44	18
57	7.53	19	17	7.30	38	18	7.22*	36*	14.2*	7.23*	33*	13.5*
58	7.50	23	21.5	7.39	36	21	7.50	25	19.5			
59	7.57	22	20.5	7.31	48	22	7.52	24	20	7.40	43	25
Average	7.52	22	18.4	7.38	31.7	18	7.46	22	16	7.29	38	17.8

*Not included in average. Patient moribund.

TABLE II. CONTROLS

PATIENT NUMBER	AFTER ANESTHESIA CHEST CLOSED			CHEST OPEN			PRIOR TO CHEST CLOSURE			AFTER CHEST CLOSURE SPONTANEOUS VENTILATION		
	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3	pH	pCO_2	HCO_3
C-1	7.38	32	18.5	7.42	29	18.5	7.38	29	18.5	7.26	44	18.5
C-2	7.37	30	17	7.48	27	20	7.41	31.0	19	7.34	39	20
C-3	7.45	26	18.5	7.47	26	19	7.45	26	18	7.27	48	20
C-4							7.47	13.5	11.5	7.25	38	16
C-5	7.43	23	15.5	7.50	16	14	7.47	18	14	7.31	30	15
C-6							7.52	19.5	16.5	7.29	37	17
C-7	7.28	50.5	22	7.52	21	18	7.43	24	16	7.32	39	19
C-8	7.35	40	21	7.52	23	19	7.57	15	15	7.30	44	20
Average	7.38	34	19	7.49	24	18	7.46	22	16	7.29	40	18

In the control group similar observations were made. While the chest was open the average carbon dioxide tension was maintained at about 22 mm. Hg. After closure it rose to 40 mm. Hg, and this was accompanied by a fall in pH from 7.46 to 7.29.

A graphic comparison of the changes that occurred in the two groups on returning to spontaneous *ventilation is shown in Fig.* 1.

The fall in pH following respiratory alkalosis is further demonstrated in Fig. 2, in which the patient showing the greatest fall in pH is illustrated. This patient, who had an interventricular septal defect with severe pulmonary hypertension, had a satisfactory postoperative course. Fig. 3 illustrates the same type of change in 1 of the control cases.

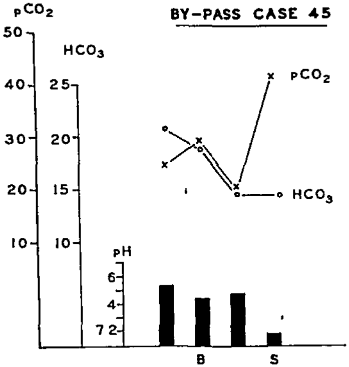

Fig 2

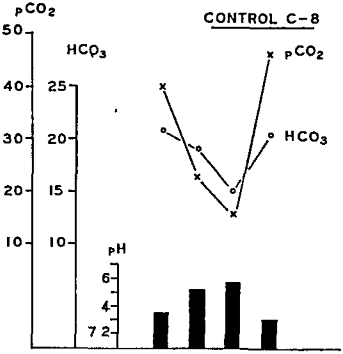

Fig 3

Fig. 2.—Biochemical changes following respiratory alkalosis in a patient undergoing ventricular septal defect repair. The solid bars from *left to right* represent pH values after opening the chest, during bypass *(B)*, prior to chest closure, and after chest closure with spontaneous ventilation (*S*). The pH dropped from 7.46 to 7.18 following return of pCO_2 to a normal level.

Fig. 3.—Biochemical changes following respiratory alkalosis in a patient undergoing ligation of a patent ductus arteriosus. The solid bars from *left to right* indicate the arterial pH before thoracotomy, after opening the chest, prior to chest closure, and after chest closure with spontaneous ventilation. When hyperventilation was discontinued, the pCO_2 rose from 15 to 44 mm. Hg, and the pH fell from 7.57 to 7.30.

DISCUSSION

The acidosis that we have observed at the end of these operations is related to the low bicarbonate values; the carbon dioxide tension has rapidly returned to a normal level but the bicarbonate has remained depressed, forcing a drop in pH. Respiratory alkalosis reduces the bicarbonate concentration partly because a portion of the carbon dioxide in the blood is present as bicarbonate,[6] and partly for reasons discussed below. The respiratory alkalosis may be assumed to be in large part responsible for the lowered bicarbonate values seen in the course of these operations in both groups of patients. As the operations proceeded, the bicarbonate dropped further. In the pump-oxygenator patients, *it dropped from 18.7 mEq. per liter after the chest was opened to 16 before* chest closure; the carbon dioxide tension was 22 mm. Hg in each sample. In the control patients, the corresponding drop was from 18 mEq. per liter to 16 without significant change in the pCO_2. This continuing depression in bicarbonate could be a compensation for the prolonged alkalosis by renal excretion of bicarbonate, or fixed acids may have accumulated. Experimentally the rate of reabsorption of bicarbonate by the renal tubules is a direct and linear function of the carbon dioxide tension.[5] As the pCO_2 falls, so does the bicarbonate reabsorption and the plasma bicarbonate concentration is thereby reduced.

Fixed acid accumulation can also result from respiratory alkalosis. Boucot and associates[4] recorded the glycolytic response to vigorous hyperventilation with increase in lactate ion. Ionic shifts in respiratory alkalosis have been studied by Elkinton,[7] who showed that an anion shifted out of the cells, which, on the evidence of Giebisch,[9] was felt to be lactate. More recently Huckabee[11] showed an increase in lactate on hyperventilation, whether active in man or passive in paralyzed animals on a ventilator. He pointed out that rapid lactic acid accumulation during hyperventilation represents a mechanism for quickly reducing body bicarbonate as an adjustment to alkalosis. Others[10] have demonstrated the same rise in anesthetized hyperventilated patients. Litwin and associates[12] pointed out the biochemical similarities between hypoxic acidosis and respiratory alkalosis, particularly the increase in lactate and chloride and the decrease in bicarbonate and potassium. The bicarbonate depression during these operations could also be due to fixed acid accumulation produced by factors other than respiratory alkalosis, notably tissue hypoxia either during normal or extracorporeal circulation.

Malette[13] has demonstrated cerebral tissue anoxia from hyperventilation in dogs. Although cerebral vasoconstriction played a part, hypoxia was mainly due to resistance of alkaline hemoglobin to release bound oxygen. The venous oxygen was therefore high despite tissue anoxia. The alkalosis in these animals was much more severe than in the patients reported herein. Should this mechanism apply at levels of alkalosis observed clinically, then venous oxygen saturation could not be taken as an indication of the adequacy of tissue oxygenation.

There seems no necessity to implicate the pump-oxygenator, however, as similar changes were seen in the control group. The bypasses in these cases were carried out with an average flow rate of 98 c.c. per kilogram per minute, and the venous oxygen saturation averaged 72 per cent, the lowest being 54 per cent. The flow rate was, therefore, adequate, and acidosis on the basis of inadequate tissue perfusion would not be expected.

All but 2 of the patients studied in this report were children. That the changes reported herein are less likely to occur in adults is a distinct possibility. We have noticed a tendency for the bicarbonate level to remain higher in adults and, therefore, the pH shift on re-accumulating carbon dioxide at the conclusion of the operation has been less profound.

Although the level of acidosis observed in these cases is mild in most instances, it is the sudden drop in pH that has concerned us. We have not observed any clinical ill effects during this period of transition from controlled to spontaneous ventilation.

SUMMARY

In a series of thoracic operations carried out with hyperventilation, the carbon dioxide tension was reduced to 22 mm. Hg. When carbon dioxide reaccumulation was permitted at the end of operation, a sudden fall in pH occurred The findings were similar in two groups of patients, one undergoing extracorporeal circulation for intracardiac surgery and the other having had other thoracic procedures All but 2 of the patients were children

The technical assistance of Miss B Thomas and Mr W Schroeder is gratefully acknowledged

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RAPID HYPOTHERMIA: AN IMPROVED EXTRACORPOREAL METHOD

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HYPOTHERMIA has been successfully employed in various forms as an adjunct to cardiac surgery—in the past by surface contact techniques,[1, 2] and more recently via the extracorporeal circulation.[3-10] The combination of hypothermia with extracorporeal circulation reduces metabolic requirements and blood flow rates, increases the efficiency of oxygenation, and enables longer safe perfusions. It allows the perfusion of large patients whose flow rate would otherwise exceed the capacity of a given oxygenator at normothermia.

Since the efficiency of both blood oxygenation and heat transfer depend on a maximum exchange surface per unit blood flow, an apparatus was developed to combine these functions within the oxygenator. This unit, which adapts to the rotating disc oxygenator, consists of a series of semicircular, stainless steel coils connected in parallel. An electronically controlled unit circulates water at the desired temperature through the coil thereby providing rapid, safe, and precise control of blood temperature.

This method of rapid hypothermia and rewarming is accomplished with total cardiopulmonary bypass and incorporates all of the prerequisites for ideal thermal regulation: (1) maximum efficiency of heat exchange, (2) precise and simple control of blood temperature, (3) safety with regard to the production of gas emboli developed during rapid rewarming, (4) no impedance to blood flow, (5) minimal injury to blood elements, and (6) no additional priming volume.

Extracorporeal hypothermia as utilized clinically today is initiated via the femoral vessels with partial bypass prior to thoracotomy. In contrast, this method effects heat exchange on total cardiopulmonary bypass without prolongation of operative time or commitment to hypothermia before the intrathoracic situation has been evaluated.

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

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EXPERIMENTAL DESIGN

To evaluate this method of thermoregulation and to study the effects of rapid total body cooling and rewarming, a series of experiments was designed. The following factors were examined: (1) the efficiency and rate of blood and body temperature change, and (2) the safety of rapid thermal alterations with regard to (a) the temperature gradient which can be applied to the blood without producing damage, (b) the effect of this apparatus on blood elements and oxygenation, (c) the formation of bubble emboli upon rapid rewarming, and (d) the blood electrolyte and pH change.

Following evaluation, this thermoregulation unit was incorporated into the extracorporeal circuit for the production of rapid hypothermia and rewarming as well as maintenance of normal temperature in human perfusions.

APPARATUS

The apparatus for extracorporeal blood thermoregulation consists of two parts: (1) a coil (Fig. 1) that conducts water and adapts to the inside of the Kay-Cross rotating disc oxygenator,[11] and (2) an electronically controlled pumping unit (Fig. 2) containing hot and cold reservoirs.

The coil is a series of ⅛ inch diameter stainless steel tubing semicircularly molded, and connected in parallel. The longitudinal inflow and outflow conduits perforate the end plates near the top and are connected to the thermoregulation pumps, reservoirs, and electronic control unit. The glass reservoir is ½ inch larger in diameter than the standard size in order to accommodate the coil and maintain the same priming volume. Coils of different lengths adapt to the 13-, 17-, and 21-inch oxygenators.

The pumping unit consists of two water reservoirs, and two centrifugal pumps which circulate fluid through the coil at a rate of 6 gallons per minute. The warming reservoir is equipped with a thermostatically controlled 2,000 watt heater and provides rapid attainment of temperatures between 0° to 60° C. The warming fluid may be internally recirculated to maintain a given temperature, or pumped through the coil. The cooling reservoir is held constant at 1° to 3° C. with ice water which is always available for coil circulation. Interlocking solenoid valves enable instantaneous shift from one reservoir output to the other, providing maximum temperature gradients for blood thermoregulation.

METHODS

Animal Investigation.—Mongrel dogs varying in weight from 11 to 22 Kg. were anesthetized with intravenous Nembutal, intubated, and mechanically respirated with 97 per cent oxygen and 3 per cent carbon dioxide. Cannulations of the right femoral artery for input of oxygenated blood and of the venae cavae, via the right atrium, for venous drainage were performed.

The oxygenator containing the thermoregulatory coil was primed with heparinized blood, drawn the previous day. A calibrated variable stroke volume

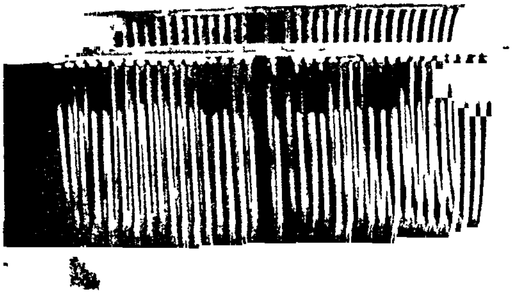

Fig. 1.—Heat exchange coil.

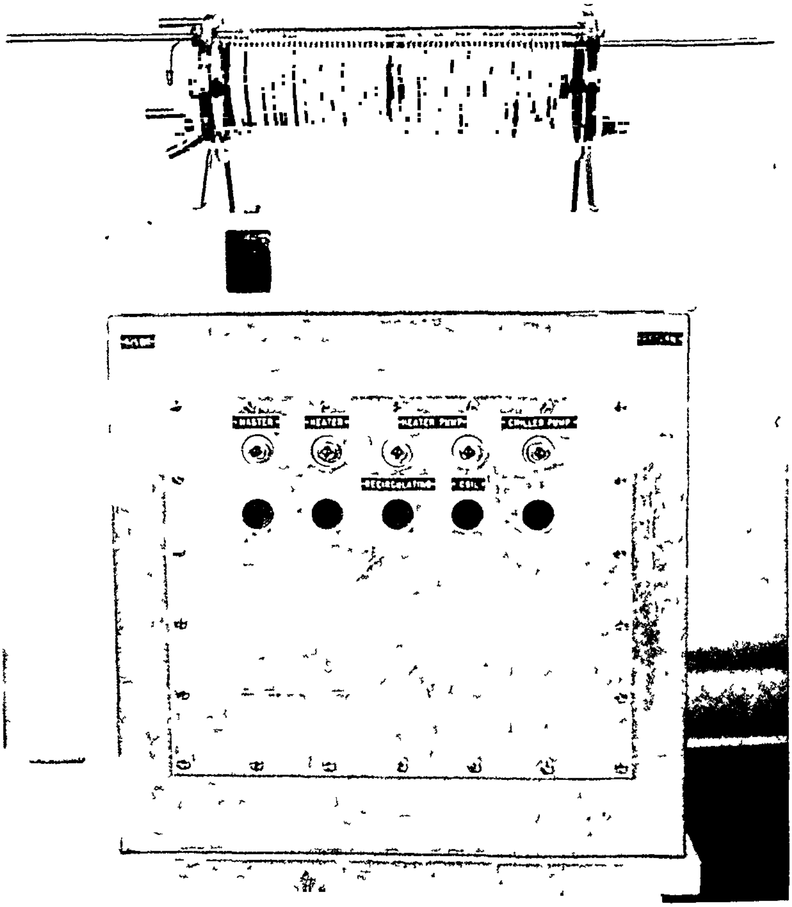

Fig. 2.—Thermoregulation unit and assembled oxygenator

and stroke rate piston-type pump with occlusive flap valves at each end of a Tygon chamber was employed. Cardiopulmonary bypass was established using gravity drainage into the oxygenator.

Animal perfusions were separated into two groups of 12 and 11 animals each. In the first group, esophageal temperature was lowered to 28° C. and in the second group to levels from 10° to 22° C.* After stabilization of pressures at a perfusion temperature of 37° C., rapid cooling was initiated with 1° to 3° C. water in the cooling circuit. When the desired level of hypothermia was achieved, the blood temperature was controlled to maintain the esophagus at that level for ½ hour. A right ventriculotomy was performed and repaired during this period. Coronary blood from the open cardiotomy was returned via a roller pump to the oxygenator. Rapid rewarming of the blood and body was then effected by circulating water at 44° C. through the coil.

Thermocouples recording on a Brown potentiometer were placed in the mid-esophagus, rectum, thigh muscle, right ventricle, as well as the venous and arterial ends of the oxygenator. Inflow and outflow coil temperatures were constantly recorded. Blood oxygenation was monitored with a Clark oxygen electrode inserted in the arterial end plate. Venous and arterial pressures were monitored via left femoral vessel cannulae.

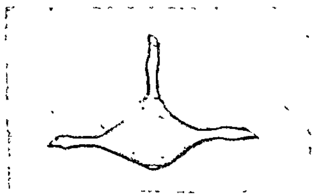

Fig. 3.—Plenum chamber.

A plenum chamber (Fig. 3) was inserted into the arterial end of the oxygenator in parallel with the outflow tract to discern any microbubbles evolved during rapid rewarming. This device provides a decrease in linear flow by virtue of increased cross sectional area, thus permitting bubbles to rise and be trapped in the top of the chamber.

Blood samples were obtained at intervals of 5 to 10 minutes from the patient and oxygenator for determination of platelets, white blood cells, plasma hemoglobin, pH, and serum Na^+, K^+ and Ca^{++}. A control aliquot was maintained at 37° C. and sampled simultaneously with the oxygenator blood samples.

To determine safe parameters for heating and cooling blood, in vitro experiments were performed on freshly drawn dog blood drawn the day of the procedure. Using siliconized equipment and exercising maximum care in blood handling, the extracorporeal circuit was primed as in the animal experiment, substituting a reservoir for the dog. A control blood sample was maintained in a 37° C. water bath.

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*Cardioplegia was produced and maintained with hypothermia at temperature levels below 20° C. Results of this investigation will be reported elsewhere.

TABLE I. THERMOREGULATION DATA FROM ANIMAL EXPERIMENTS

DOG	WEIGHT (KG.)	FLOW COOLING (C.C./KG.)	ESOPHAGUS RATE COOLING (°/MIN.)	MIN. ESOPHAGUS TEMP. (°C.)	MIN. BLOOD TEMP. (°C.)	RATE BLOOD COOLING (°/MIN.)	FLOW WARMING (C.C./KG.)	ESOPHAGUS RATE WARMING (°/MIN.)	RATE BLOOD WARMING (°/MIN.)
24	22.2	54	0.70	28	18	13	50	0.21	1.6
25	22	55	1.38	25	14	11	55	0.27	1.8
37	16	75	2.00	28.5	10	9	60	0.90	1.2
38	11	68	1.00	29.4	9	11	54	0.47	4
40	18	77	2.00	28.6	20	16	55	0.63	5
41	20	100	1.50	26.8	19	10	60	0.65	1.4
42	14.5	90	1.30	28	16	11	65	0.50	2
43	11	90	2.30	29.5	16	12	90	1.0	6
57	16	63	0.90	31.5	13	14	63	0.33	5
60	14	21	0.70	26.5	8	15	43	0.33	6
61	18	67	1.0	25.5	16	11	83	1.0	7
62	16	44	1.0	27	13	10	44	0.47	4
26	18	78	2.30	22	12	10	78	0.75	2.5
27	13	45	0.95	21	5	11	45	0.33	2.6
28	13	38	0.65	21	5	16	23	0.24	4.3
29	13	50	1.30	11.6	3	7	38	1.0	9
30	20	55	1.16	22.8	13	7	60	0.6	3
31	13	46	1.00	24	9	6.5	69	0.55	2.5
32	13	77	1.10	24.6	8	13	38	0.55	6
59	18	120	1.75	16	15	11	93	0.88	5
63	14	29	1.0	22.5	12	7	43	0.63	5
64	13.5	45	2.0	15.5	14	16	45	0.83	8
65	23.6	85	2.9	11.5	6	11	55	0.90	8

For determination of the critical upper thermal limit, blood was circulated at 37° C and then raised 1° every 5 minutes to a temperature of 50° C. At the end of each 5 minute period, a sample was taken from the oxygenator and the control for the determination of plasma hemoglobin, white blood cells, and platelets. Varying temperatures of coil fluid were utilized to establish safe limits for blood contact. When the temperature at which the blood began to exhibit damage had been determined, fresh blood was placed in the bypass circuit. It was circulated for 20 minutes at each degree of temperature beginning 3° below and increasing through the thermal level producing damage. In this way the safe upper limit of blood temperature in the extracorporeal circuit was determined as well as the optimum water temperature gradient which could safely be applied to the coil.

To investigate the lower thermal limit, blood at 37° C was exposed to a coil temperature of 1.5° C with the animal in the circuit. The blood rapidly dropped to 4° C where it was maintained for one half hour. Since blood elements were not damaged in excess of control values it was unnecessary to continue these experiments in vitro.

RESULTS

Experimental Results.—Twenty three mongrel dogs were subjected to rapid body cooling and rewarming. Blood flow rates were different from animal to animal and varied with temperature (Table I). Maximum rates of cooling were 16° C per minute for blood and 2.9° C per minute for the esophagus. The velocity of rewarming was slightly less than that of cooling with a maximum blood rate of 9° C per minute and an esophageal rate of 1.0° C per minute. Once the desired temperature level was reached it was possible to control it within ±0.5° C.*

The rates of cooling and rewarming were directly proportional to the rate of flow as is shown in Figs. 4 and 5. When the esophageal temperature was lowered the venous return to the oxygenator decreased. At 30° C, it was approximately 50 per cent of the flow at normothermia. Consequently, the more rapid changes of temperature occurred in the higher temperature ranges with regard to the flow effect. This factor operated independently of the gradient advantage available in the water bath, which enabled an increased rate of cooling, but a decreased rate of rewarming.

It was also observed that even with similar blood flow rates per unit of weight and identical blood temperature changes, different animals occasionally cooled at dissimilar rates. The viscosity of the blood increased with the decrease in temperature and blood flow.

Efficiency of this heat exchange unit can be calculated in the following manner:

$$\text{Efficiency} = \frac{\text{Blood temperature rise or fall}}{\text{Temperature of inlet blood} - \text{Temperature inlet } H_2O} \times 100$$

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*These limits of control were corroborated when the unit was employed for maintenance of normothermia in 60 animal and 10 clinical patients.

The efficiency of cooling and warming is approximately 70 per cent. However, the velocity of warming is lower because of the thermal gradient to which blood can safely be exposed. The efficiency varies slightly with the blood flow through the oxygenator (Fig. 6) but is not significantly affected by changes in disc rotation or rate of oxygen flow.

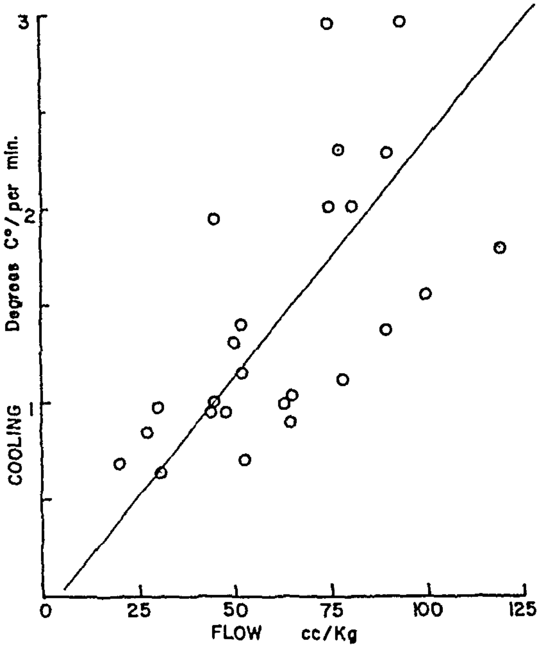

Fig. 4.—Effect of blood flow rate on esophageal cooling.

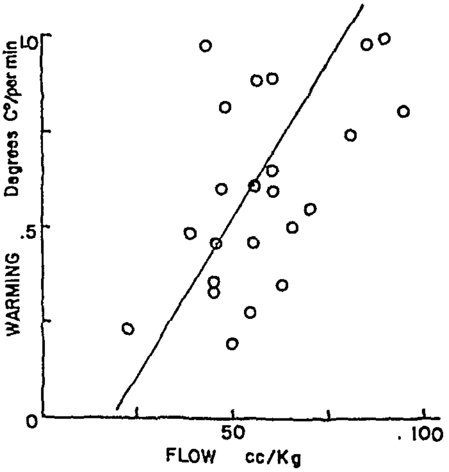

Fig. 5.—Effect of blood flow rate on esophageal warming.

Direct blood heat exchange provides for uniform rapid cooling and warming of the vital organs, the esophagus responding immediately and the heart following at a somewhat slower rate (Fig. 7). Both closely parallel the blood temperature change. The skeletal muscle of the thigh changes at a much slower rate and never attains the internal organ temperature within the duration of our experiments. The rectal temperature has been found to be

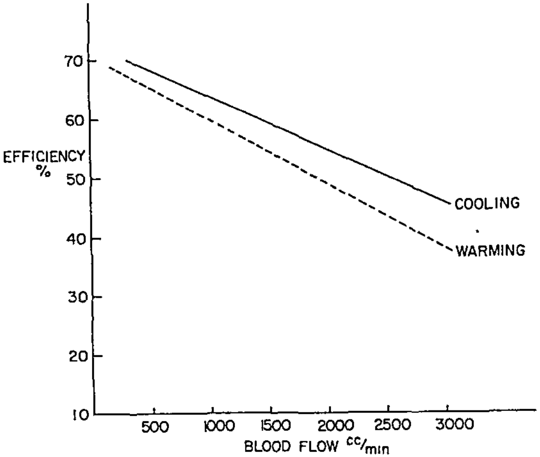

Fig 6 —Efficiency of thermoregulation with varying blood flow rates.

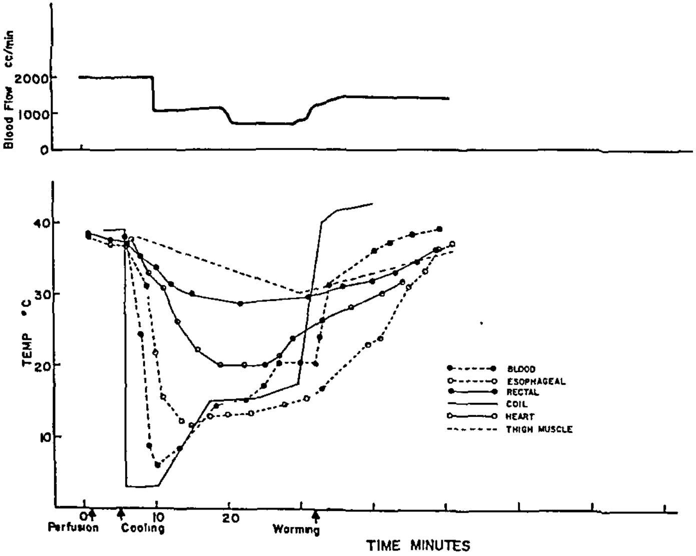

Fig. 7.—Temperature and flow record of typical animal hypothermia experiment

the most variable in its rate of temperature change, with the final stabilized thermal level between that of the vital organs and the muscle.

Utilizing 1.5° C. water in the coil, a blood temperature of 4° C. was achieved consistently without any significant change in blood elements from the normothermic controls.

The in vitro investigation revealed the upper thermal limit to be a coil temperature of 45° C. which produced a blood temperature of 43.5° C. At coil temperatures above 45° C., considerable hemolysis and thrombocytopenia occurred. With coil temperatures of 43° to 45° C., circulation of blood for 20 minutes disclosed no increase of blood damage with increased time (Fig. 8).

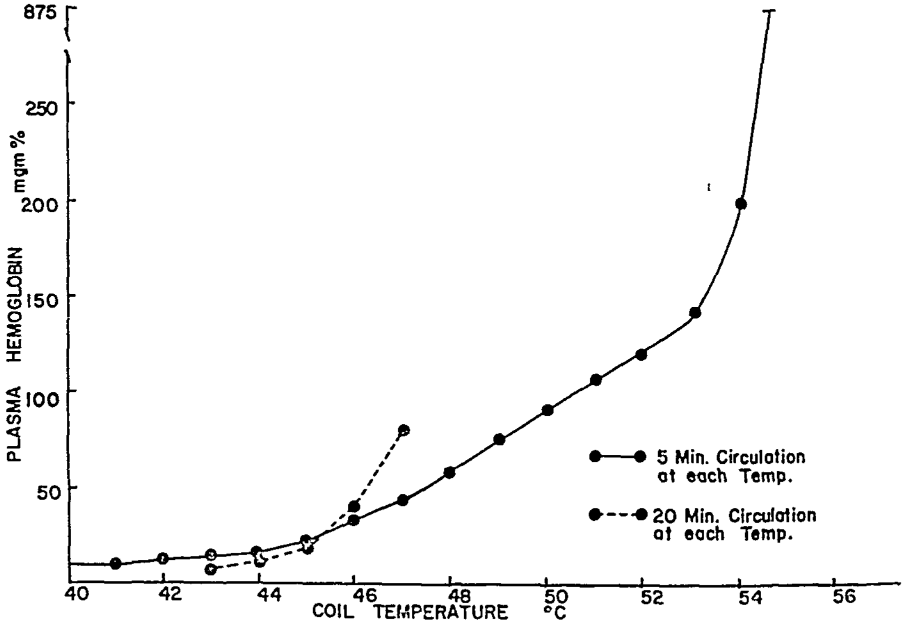

Fig. 8.—Effect of temperature on plasma hemoglobin production.

On the basis of these findings, coil temperatures of 44° C. were employed throughout our experiments as the upper thermal limit for rewarming with the maintenance of excellent blood element values (Table II). No significant difference was noted from the control normothermic perfusions (Table III) and therefore it is concluded that rapid cooling and rewarming within the limits established, are completely safe in regard to blood element damage.

The higher ranges of blood destruction occurred in cases with large coronary sinus suction return. Perfusion durations up to 180 minutes without coronary sinus blood suctioning were associated with an average increase of only 20 mg. per cent plasma hemoglobin.

Serum electrolyte determinations on the serial blood samples revealed no significant changes of Na^+, K^+, or Ca^{++} during hypothermia or rewarming. There was some depression of pH during hypothermia to levels from 7.18-7.28, but at the close of perfusion pH was always within normal limits.

The presence of the thermoregulatory coil within the oxygenator permitted the blood level to fall as low as 1½ inches below the recommended level

TABLE II BLOOD ELEMENT DAMAGE DURING 60 MINUTE EXTRACORPOREAL CIRCULATION WITH RAPID COOLING AND REWARMING

	RANGE	AVERAGE
Plasma hemoglobin (increase)	5 90 mg %	38 mg %
Platelets (decrease)	50,000 250,000	110,000
WBC (decrease)	2,000 5,000	2,600

TABLE III BLOOD ELEMENT DAMAGE DURING 60 MINUTE NORMOTHERMIC EXTRACORPOREAL CIRCULATION

	RANGE	AVERAGE
Plasma hemoglobin (increase)	3 110 mg %	41 mg %
Platelets (decrease)	65,000 210,000	120,000
WBC (decrease)	1,900 6,000	2,900

without foaming or frothing Without the coil, marked foaming occurred with as little as ½ inch drop below the optimum level Thus, the critical problem of maintaining blood level was minimized Oxygenation of the blood was in no way compromised by utilization of the coil

Bubble formation during rapid rewarming did not present a major problem In 2 of the 23 cases, small bubbles were noted in the plenum chamber at the end of the experiment, however, these 2 animals presented no neurological deficits and were long term survivors

In this series of 23 animals, all survived at least 18 hours Fourteen were considered long term, surviving longer than 72 hours No neurological symptoms were present in any animal and all deaths were unrelated to the hypothermia

Clinical Results—This method has been successfully employed clinically for total extracorporeal hypothermia in 12 patients and for maintenance of normothermia in 5 others at the Naval Hospital, Bethesda, Maryland The same evaluation and monitoring apparatus used in the laboratory were incorporated in its clinical application

The decision to use hypothermia was made following thoracotomy and after total cardiopulmonary bypass had been instituted Duration of perfusion ranged from 30 to 52 minutes No additional operative or perfusion time was required for the cooling or rewarming

In these cases the esophageal temperature was lowered 1 0° to 2 6° C per minute and was rewarmed 0 5° to 1 0° C per minute Esophageal temperatures were maintained at 28° to 29° C The average plasma hemoglobin increase was 35 mg per cent and the platelet decrease was 50 per cent of preoperative values

DISCUSSION

This type of extracorporeal thermoregulation provides a highly efficient and safe method for rapid total body cooling and rewarming It supplies the cardiovascular surgeon with immediate hypothermia at any time during an operation without committing him to it preoperatively Minimal operating time need be wasted cooling and rewarming Rapid cooling can be effected in cases of unexpected high flows which exceed the capacity of the oxygenator If cerebral emboli are suspected during a procedure, protection with immediate hypothermia is available.

Increased efficiency of body cooling and rewarming is achieved by utilizing this apparatus within the oxygenator. This, also, eliminates additional units in the circuit with their increased impedance to blood flow and larger priming volume. Maximum safety is achieved because the oxygenator serves as a bubble trap for any gases released during rapid rewarming, and the coil permits wider fluctuation of the blood level without frothing.

The higher velocity of cooling (2.9° C. per minute) compared to rewarming (1.0° C. per minute) is largely due to the greater gradient which can be applied in cooling. Coil temperature of 1.5° C. applied to 37° C. blood yields a 33.5° C. differential operating in favor of the desired temperature change. However, a 44° C. coil temperature contacting 20° C. blood during rewarming allows only a 24° C. gradient. In addition, warming must overcome the effect of 25° C. room temperature. The normal temperature regulation mechanism of the animal does not play a large role with this "core" method of thermoregulation. With the high efficiency of heat exchange, the larger flows per unit weight produce faster rates of "core" temperature change (see Figs. 4 and 5). Total weight seems to make no difference within the range employed. Application for clinical hypothermia in 70 Kg. patients has produced equal or faster rates of temperature change than in animals. Differences in the cooling or rewarming rate of animals with the same weight, blood flow, and inflow blood temperature may be due to variations in vasoconstriction or in fat distribution.

The 50 per cent reduction of blood flow in the extracorporeal circuit below 30° C. is substantiated by the observation of King and Bounos[12] that cardiac input is 48 per cent of the normal at that temperature.

The "core" method of hypothermia cools the vital organs rapidly and the muscle mass slowly. Thus, the more vascular organs with high oxygen demands are afforded hypothermic protection early which is an advantage over the surface cooling techniques.

During hypothermia, the cooler, more viscous blood decreases the output of the Tygon pumping bag in our system approximately the same amount as the venous inflow to the oxygenator is reduced. This eliminates the necessity for change in the pump control settings during cooling or rewarming despite the marked variation of blood flow.

The theoretical possibility that dissolved oxygen will come out of solution on rapid blood rewarming and produce emboli is based on the fact that the solubility of a gas is inversely proportional to the temperature; that is, at 2° C., twice as much oxygen is soluble in plasma as at 37° C. The plenum chamber was employed because it is the most sensitive method of detecting microscopic bubbles in a flowing stream, according to Maloney.[13] Our experiments substantiated this fact, since the direct examination of blood film with a microscope or the decompression of organs proved cumbersome and less reliable.

Neither of the animals in which small bubbles were demonstrated in the plenum trap during rapid rewarming exhibited neurological signs. Since this represents only 9.1 per cent of our series and both of these animals were long-term survivors, it is concluded that rapid blood rewarming, providing it is done within an oxygenator, is safe In clinical use, a maximum gradient of 20° C has been utilized in order to remain well within the limits of safety

SUMMARY

1 A highly efficient method for direct blood cooling and rewarming, utilizing the rotating disc oxygenator and employing an electronically controlled thermoregulation unit, has been presented

2 Blood temperatures are reduced at 16° C per minute and rewarmed at 9° C per minute with precise control and safety Esophageal temperatures may be lowered 2 9° C per minute and rewarmed 1 0° C per minute

3 Successful clinical application of this method for rapid hypothermia produced with total cardiopulmonary bypass has been made in 5 patients

4 Blood may be exposed to temperatures of 1° C for cooling and temperatures of 45° C for warming without significant blood element damage

5 Rapid rewarming of cold oxygenated blood does not produce experimentally or clinically significant gas emboli with this method

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THE CLINICAL USE OF POLYBRENE AS AN ANTIHEPARIN AGENT IN OPEN HEART SURGERY

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INTRODUCTION

The use of extracorporeal circulation demands that the blood of the patient be reliably anticoagulated. The agent commonly used is heparin. It is, of course, necessary to re-establish the clotting mechanism at the end of the bypass period. Until recently, the only antiheparinic agents available were protamine (Salmine) sulfate and toluidine blue. Now a new agent is available which shows considerable clinical promise. The purpose of this paper is, first, to review mainly the undesirable effects of protamine, and, second, to review our clinical experience with the newer agent, Polybrene.*

THE ANTIHEPARIN ACTIVITY OF PROTAMINE (SALMINE) SULFATE

The antiheparin activity of protamine was described as early as 1937 by Chargraff and Olson,[1] but was not clinically employed until heparin was employed more vigorously in the treatment of various thromboembolic phenomena. The need for rapid reversal of the anticoagulant effect of heparin was seldom necessary. However, the advent of open heart surgery, utilizing cardiopulmonary bypass techniques, has brought with it the need for rapid reversal of heparin effect, and thus the widespread use of protamine.

Although protamine is usually an effective agent, there are several factors worthy of mention which render it less than ideal. First, and requiring little explanation, the relative instability of the preparation is an undesirable quality. Second, the paradoxical anticoagulant activity of protamine places upon the physician the onus of relatively accurate calculation of dosage by rather laborious methods. This anticoagulant effect of protamine seems multifaceted. Portman and Holden,[2] and Hougie[3] demonstrated that protamine interferes

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with the conversion of prothrombin into thrombin. Hougie states that, in low concentration, protamine is antithromboplastinogenic. These authors also describe the inactivation of fibrinogen by protamine. This reaction presumably takes place by the formation of a soluble protamine-fibrinogen complex. The complex thus formed is somewhat analogous to that formed in the interaction of the macromolecular plasma expanders (polyvinylpyrrolidone, Dextran) and fibrinogen. Jacques,[4] in 1949, verified that, up to a certain level, protamine reverses the anticoagulant effect of heparin, but beyond this level, it seems to enhance the heparin effect.

Third, Jacques further demonstrated that the rapid infusion of protamine causes a marked fall in the blood pressure, probably as a result of the extensive dilatation of muscular arterioles. This fall in blood pressure is sometimes resistant to therapy in experimental animals and seems increased in those who have undergone extracorporeal circulation.[5] Jacques also reported the transient leukopenia and thrombocytopenia following the injection of protamine. The extent of the deleterious nature of this reduction in number of formed elements of the blood is unclear.

Fourth, it would be desirable to have an antiheparin agent which would exert an in vivo anticoagulant effect more quickly than protamine. Although in vitro the reversal of heparin with protamine is instantaneous, limitations in the rate of administration delay the in vivo appearance of clotting.

A fifth criticism of protamine rests with the varying potency of the preparation. This factor renders the establishment of standard doses virtually impossible. Portman and Holden found that the protamine/heparin ratio in vitro varied from 16:1 to 0.7:1.0, depending upon the particular lot of protamine used.

With these inadequacies in mind, several relatively satisfactory methods have been suggested to estimate the amount of protamine required to reverse the heparin effect. All of these are variants of the titration techniques. These techniques, however, are time consuming, and thus constitute another criticism to the clinical use of the preparation.

A BRIEF DESCRIPTION OF POLYBRENE

It is understandable that the description of a new antiheparin agent in 1953 was welcomed.[5] This material, Polybrene, is a stable quartenary ammonium salt with a formula $(C_{13}H_{30}Br_2N_2)_x$, a polymer of N,N,N^1,N^1 tetramethylhexamethylenediamine and trimethyl bromide. It shares features with both protamine and toluidine blue. It exerts a potent antiheparin effect both in vivo and in vitro. It is also in itself an anticoagulant.

A clinical and experimental trial of Polybrene has been reported by Weiss and his associates.[7] This group concluded that the agent is superior to protamine and toluidine blue. They reported rapid conversion to a normal clotting time, with minimal side effects. These include dizziness, thought to be secondary to a transient hypotension from too rapid administration. The authors also considered the possible antigenic role of Polybrene, and advised against its use in patients with a history of allergic response.

TABLE I. A SUMMARIZATION OF THE USE OF POLYBRENE TO REVERSE THE HEPARIN EFFECT IN 47 PATIENTS

NO.	WT. (KG.)	HEPARIN (MG.)	POLYBRENE (MG.)	RATIO HEPARIN/ POLYBRENE	TIME BETWEEN HEPARIN AND POLYBRENE (MIN.)	MIN. AFTER POLYBRENE TO CLOTTING TIME DETER.	CLOTTING TIME (MIN.)	REMARKS
1	43	50	35	1.4/1	—	10	10	No reaction
2	15	30	21	1.4/1	—	10	9	No reaction
3	56	170	120	1.4/1	—	(a) 30 (b) 55	(a) 75 (b) 20	Given additional 50 mg. Polybrene No reaction
4	54	160	115	1.4/1	—	(a) 30 (b) 60	(a) 25 (b) 6	Stridor, general rash; I.V. Benadryl Additional 20 mg. Polybrene
5	41	124	100	1.2/1	—	75	16	No reaction
6	15	45	40	1.1/1	—	10	12	No reaction
7	52	160	120	1.4/1	—	10	13	No reaction
8	66	210	150	1.4/1	—	(a) 10 (b) 55	(a) 21 (b) 11	No reaction Additional 60 mg. Polybrene
9	—	180	140	1.3/1	—	15	15	No reaction
10	—	150	130	1.2/1	90	15	25	Additional 50 mg. Polybrene
11	—	190	190	1.0/1	—	15	7	No reaction
12	12	96	60	1.6/1	—	(a) 15 (b) 45	(a) 18 (b) 5	No reaction Additional 30 mg. Polybrene
13	58	180	180	1.0/1	110	15	15	No reaction, patient on lipoheparin preop.
14	20	60	60	1.0/1	60	20	7	No reaction
15	56	170	170	1.0/1	127	(a) 25 (b) 60	(a) 26 (b) 23	Patient with severe clotting disorder; given 32 L. whole blood, additional 170 mg. Polybrene
16	70	240	240	1.0/1	190	15	5	No reaction
17	6	20	20	1.0/1	96	15	8	No reaction
18	56	170	170	1.0/1	87	10	20	No reaction
19	26	80	80	1.0/1	73	20	5	No reaction
20	65	210	210	1.0/1	125	20	8	No reaction
21	60	200	200	1.0/1	210	18	12	No reaction
22	60	200	200	1.0/1	155	15	10	No reaction
23	48	150	150	1.0/1	90	20	10	No reaction
24	62	150	150	1.0/1	95	15	6	No reaction
25	8	30	30	1.0/1	100	(a) 25 (b) 55	(a) 25 (b) 10	No reaction Additional 10 mg. Polybrene
26	55	170	170	1.0/1	85	20	8	No reaction
27	24	80	80	1.0/1	75	15	15	No reaction
28	33	100	100	1.0/1	80	15	8	No reaction
29	80	240	240	1.0/1	66	(a) 15 (b) 45	(a) 30 (b) 8	Additional 100 mg. Polybrene, urticarial rash, I.V. Benadryl
30	50	160	160	1.0/1	65	15	15	No reaction
31	42	150	150	1.0/1	89	20	10	No reaction
32	72	220	220	1.0/1	85	15	9	No reaction
33	11	33	33	1.0/1	105	15	7	No reaction

TABLE I—CONT'D

NO	WT (KG)	HEPARIN (MG)	POLYBRENE (MG)	RATIO HEPARIN/ POLYBRENE	TIME BETWEEN HEPARIN AND POLYBRENE (MIN)	MIN AFTER POLYBRENE TO CLOTTING TIME DETER	CLOTTING TIME (MIN)	REMARKS
34	29	90	90	1.0/1	168	15	9	No reaction
35	10	30	30	1.0/1	95	20	9	No reaction
36	37	120	120	1.0/1	100	15	10	No reaction
37	32	110	110	1.0/1	81	(a)15 (b)35	(a)25 (b)10	No reaction Additional 50 mg Polybrene
38	74	230	230	1.0/1	177	15	8	No reaction
39	47	140	140	1.0/1	75	15	7	No reaction
40	45	140	140	1.0/1	90	15	8	No reaction
41	52	160	160	1.0/1	75	15	7	No reaction
42	24	70	70	1.0/1	95	15	8	No reaction
43	53	160	160	1.0/1	60	15	13	No reaction
44	68	200	200	1.0/1	75	15	15	No reaction
45	82	200	200	1.0/1	95	15	8	No reaction
46	28	60	60	1.0/1	20	15	7	No reaction
47	91	300	300	1.0/1	175	15	5	No reaction

Five factors indicate that Polybrene has many advantages over the older antiheparinic agents: (1) its stability, (2) its apparent more rapid action, (3) the apparent greater margin of safety between doses which have a good antiheparin effect and those which might exert a synergistic anticoagulant activity, (4) the uniform potency of the preparation from one lot to another, and (5) the absence of severe hypotensive reactions.

THE CLINICAL USE OF POLYBRENE

In the first 52 cases of open heart surgery done at this institution, protamine was routinely used to reverse the heparin effect. In view of the encouraging factors already reviewed concerning Polybrene, beginning over a year ago that preparation has been used exclusively as an antiheparin agent in patients undergoing open heart surgery. It has now been employed in 47 cases, a summary of which has been tabulated in Table I. Although a careful record of the clotting time was not routinely kept when protamine was employed, these clotting times were frequently prolonged after heparin effect reversal, regardless of the amount of protamine used. In contrast, the rapidity and consistency of reversal of the heparin effect by Polybrene has been striking.

In the first 12 cases, a heparin/Polybrene ratio (milligram to milligram) of 1.4:1.0 was employed. This was in accord with the ratio suggested by Preston and others.[6] However, in 9 of these cases, the clotting time, as determined by a modified Lee and White technique, was greater than 10 minutes, when measured from 10 to 25 minutes after the administration of the Polybrene. In 5 of these cases, the clotting time was sufficiently prolonged (up to 75 minutes), and the patient's bleeding of such a magnitude, that additional Polybrene was given (up to 60 mg.). In these 9 cases, the second determination of the clotting time was satisfactory, and the patient showed evidence of clotting clinically. These augmenting doses were noted to bring the heparin/Polybrene ratio to 1.0:1.0. Consequently, since that experience, Polybrene has been administered on a milligram per milligram basis with heparin.

Although some observers have reported a transient, albeit sometimes rather marked hypotension following the intravenous administration of Polybrene, the phenomenon has not been observed with constantly monitored arterial pressures. An attempt has been made to give the calculated dose slowly into the infusion line over a period of approximately 5 minutes. In a few instances, however, this period has been substantially reduced without any untoward effect being noted.

In the last 35 cases, supplemental Polybrene was given in four instances. The first, Case 15, was a 19-year-old boy with a tetralogy of Fallot, who had previously undergone a Blalock procedure. One hundred and seventy milligrams of heparin was administered for anticoagulation followed by a like amount of Polybrene 127 minutes later. Bleeding from all areas of the incision however, continued to be massive; and the clotting time, as measured 25 minutes after Polybrene administration, was 26 minutes. An additional 170 mg. of Polybrene was given, yet 20 minutes later the clotting time was 25 minutes. During this period, the sternotomy incision was re-opened in an attempt to control local bleeding points. It was obvious that a diffuse hematologic defect existed. A *total* of 32 L. of fresh whole blood was given to this patient. He died with continued massive blood loss, in spite of fresh blood, fibrinogen, vitamin K, steroids, and adrenochrome semicarbazone. This bleeding diathesis was evident prior to administration of Polybrene, and, in view of the massive transfusions necessitated by continued blood loss, this case cannot be regarded as a Polybrene failure. The hemorrhagic disorder could not be clearly defined by the hematologists prior to the patient's death.

A second instance in which additional Polybrene was given was that of Case 29, a 33-year-old man weighing 80 kilograms, who had a ventricular septal defect. Two hundred and forty milligrams of heparin was administered 66 minutes before the patent received an equal amount of Polybrene. The clotting time, as measured 15 minutes after the administration of Polybrene, was 30 minutes. He received an additional 100 mg. of the agent (total dose—340 mg., or 4.25 mg./Kg.), with a second clotting time determination of 8 minutes. Shortly after receiving the supplemental Polybrene, this patient developed a generalized urticarial rash, which rapidly cleared. This reaction cannot be clearly connected to the Polybrene, as the continued bleeding had necessitated the administration of considerable blood subjected to a 10-minute emergency crossmatch. The postoperative course was without incident.

Another case which warrants mention is that of a 20-year-old woman with an uncomplicated atrial septal defect (Case 4). She received 160 mg. of heparin prior to cardiopulmonary bypass, followed by 115 mg. of Polybrene at decannulation Restoration of a normal coagulation mechanism was prompt and lasting However, the patient developed a generalized erythematous papular rash and a minimal stridor These complications were first noted 45 minutes after administration of Polybrene, when the drapes were removed and the patient extubated It was thought that the stridor was possibly due to vocal cord trauma at the time of intubation, or to drug or transfusion reaction Because it was believed that if this respiratory difficulty became worse on the ward the patient's life might be compromised, a tracheostomy was performed while she remained in the operating room Shortly thereafter, on occlusion of the tracheostomy tube, no stridor was noted When the tube became dislodged after a forceful cough that evening, it was decided to leave it out Again, the convalescent period was uneventful

The other patients requiring an additional amount of Polybrene received it without incident, with a rapid reversion to a normal clotting time There have been no instances other than the rather inconclusive ones described above of any reaction associated with Polybrene administration In one instance, Case 46, that of a child found to have an inoperable congenital lesion upon digital exploration of the heart, the antagonistic dose of Polybrene was given just 20 minutes after an equivalent amount of heparin The clotting time, as measured 15 minutes later, was just 7 minutes As seen in Table I, the clotting time, measured 15 minutes after Polybrene administration, has been consistently below 15 minutes and, in 80 per cent of cases, under 10 minutes

SUMMARY

Protamine reversal of the anticoagulant effect of heparin was used in approximately the first half of 100 patients undergoing open heart surgery at this institution In the last 47 patients, Polybrene has been utilized for this purpose The superiority of Polybrene seems unequivocal

The clotting time, measured 15 minutes after Polybrene administration, was between 5 to 10 minutes in 80 per cent of the patients, and consistently below 15 minutes in all patients without complicating factors Two patients developed a maculopapular rash not clearly related to Polybrene administration Both responded readily to intravenous Benadryl The ratio of 1 0 mg of Polybrene to 1 0 mg of heparin has been most effective Only occasionally has additional Polybrene been necessary to obtain the desired effect

The main advantages of this drug over others with similar action are fivefold (1) stability, (2) its apparent more rapid action, (3) the apparent greater margin of safety between doses which have a good antiheparin effect and doses which might exert a synergistic anticoagulant effect, (4) the uniform potency of the preparation, and (5) the absence of severe hypotensive reactions

The combination of these attributes and this experience indicate the value of Polybrene in open heart surgery, and whenever rapid complete reversal of the heparin effect is desired It is now routinely used in this clinic for this purpose

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EXPERIMENTAL STUDIES WITH EXTRACORPOREAL CIRCUITS AS A METHOD TO ENABLE SURGICAL ATTACK ON THORACIC ANEURYSMS

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Since Gross's work with aortic coarctation[1, 2] a decade ago, surgeons have been occupied devising reconstructive surgical procedures to deal with diseases of the thoracic aorta. While the generous collateral circulation around a coarctation allows clamping of the aorta proximal and distal to the lesion and performance of surgery in a dry field without urgency, the absence of collateral circulation about aneurysms or acute lesions of the thoracic aorta poses two major problems which become increasingly significant the closer to the heart the aorta is clamped. The first is the problem of ischemic injury to structures supplied by the aorta, distal to the point of occlusion. The second is the effect of occlusion on proximal structures, that is, hypertension in the proximal aorta, left ventricular strain, and embarrassment of coronary flow if the occluding clamp is very close to the heart. Bahnson[3] was able to sidestep these difficulties in certain thoracic aortic aneurysms by performing reconstructive aneurysmorraphy with a lateral nonoccluding aortic clamp. This method, however, will be effective only in truly saccular aneurysms and, because of lack of aortic control, may lead to difficulties where the aneurysm has eroded into adjacent structures. Cooley and his associates[4] have been able to resect and replace segments of aortic arch by the use of shunts sutured to the ascending aorta, bypassing the lesion, but this limits access to ascending aortic lesions. They have also dealt with lesions of the proximal aorta by use of the pump oxygenator and total body perfusion.[5, 6] This complicates the procedure by the addition of a mechanical oxygenator although the patient's own lungs remain potentially useful. This group has exploited the patient's lungs in lesions of the descending aorta by pumping directly from the left auricle to the femoral artery, omitting the oxygenator, but has confined the use of this technique to bypass of the distal thoracic aorta.[6, 7]

The present animal study was undertaken to evaluate various methods of shunting or pumping blood past isolated segments of thoracic aorta, considering separately the descending aorta, the entire aortic arch, and the ascending aorta

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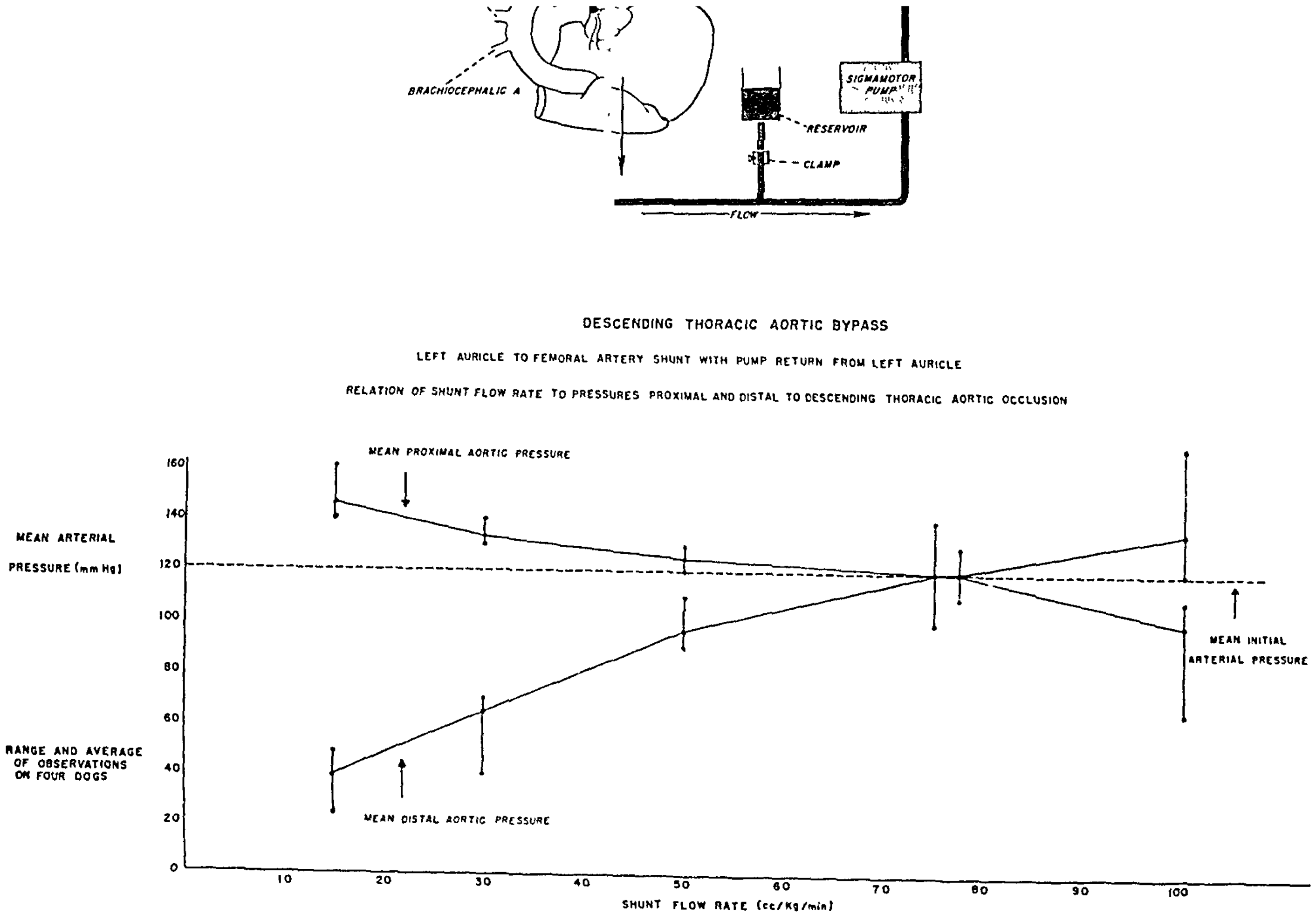


Fig. 1.—*Descending thoracic aortic bypass employing a left auricle to femoral artery shunt with pump return from the left auricle.* By this system oxygenated blood is removed by active suction from the left auricle and supplies the distal visceral structures via the femoral artery. The aorta proximal to the point of obstruction is perfused as in the normal. It is possible to obtain physiologic flows and essentially normal pressures proximal and distal to the point of aortic occlusion, by this method.

This requires determinations of the rate of shunt flow needed to perfuse structures distal to the point of obstruction and to decompress the proximal aorta without depriving it of too much blood In each of the three aortic levels, the shunting method most simple and feasible for human work was sought

METHOD

Mongrel dogs were anesthetized with Pentothal (thiopental sodium) and prepared by the administration of 1 5 mg heparin per kilogram of body weight In all dogs, the duration of aortic occlusion and bypass was 90 minutes In survival experiments the dog was considered intact if, at the end of 1 week, the behavior and activity of the dog were grossly normal, and if creatinine clearance and maximal osmotic concentrating power of the kidneys were comparable to preoperative values Mean arterial pressures were determined proximal and distal to the point of aortic occlusion by either pressure transducers and recording equipment, or simply by measuring with an aneroid pressure gauge connected to the vessel through an air column Shunt flows were measured by passing the shunted blood through a calibrated Sigmamotor pump The relations between pressure and flows in such experiments were greatly affected by reflex alterations in vasomotor tone These changes were minimized by carrying the animals at deep levels of anesthesia For similar reasons, effort was made to maintain the dog's blood volume at its initial level, erring on the high side

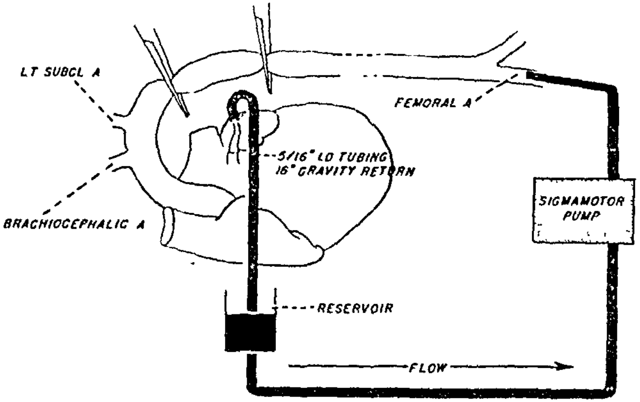
Free hemoglobin was determined immediately after the runs by the spectrophotometric method described by Hunter, Grove Rasmussen, and Soutter[8]

Descending Aorta Bypass—

Four shunting arrangements were tested (1) actively pumping from the left auricle to the femoral artery with the application of suction to the left auricle, (2) gravity flow from the left auricle to a reservoir, thence pumping to the femoral artery, (3) actively pumping from the subclavian artery to femoral artery, with the application of suction to subclavian artery catheter, and (4) simple subclavian artery–femoral artery shunt

1 *Left auricle to femoral artery shunt with pump return from the left auricle* This apparatus is shown in Fig 1 Oxygenated blood is actively pumped from the left auricle to the femoral artery by applying suction to the left auricle with a Sigmamotor pump An emergency reservoir, attached by a T connection to the inflow side of the pump and ordinarily clamped off, is not essential, but is a convenient means of rapid transfusions with donor blood or with blood recovered from the subject

Fig 1 shows the effect of varying shunt flow rate on mean arterial pressure, proximal and distal to the point of aortic occlusion It will be noted that these two pressures are equal and also approximate the aortic pressure before occlusion at a flow of about 75 c c /Kg /min , which presumably defines unobstructed flow at this level in the aorta Flows less than this ideal are allowable



DESCENDING THORACIC AORTIC BYPASS

LEFT AURICLE TO FEMORAL ARTERY SHUNT WITH GRAVITY RETURN FROM LEFT AURICLE

MEAN PRESSURE (mm Hg) DATA, SHUNT FLOW, AND SURVIVAL RESULTS FOR NINETY MINUTE DESCENDING THORACIC AORTIC BYPASS

DOG NO	MEAN PRESSURE IN PROXIMAL AORTA		MEAN PRESSURE CHANGE IN PROXIMAL AORTA	MEAN PRESSURE IN DISTAL AORTA		MEAN PRESSURE CHANGE IN DISTAL AORTA	FLOW IN SHUNT cc/Kg/min	SURVIVALS	COMPLICATIONS					Hgb. CONC AT NINETY MINUTES (mg %)
									NEURO-LOGICAL	UROLOGICAL				
										CONC. POWER (mosm/L)		CREAT. CLEARANCE (cc/min)		
	BEFORE BYPASS	DURING BYPASS		BEFORE BYPASS	DURING BYPASS					PRE-OP	POST-OP	PRE-OP	POST-OP	
5	130	145	+15	130	40	-90	30	YES	normal	2000	2200	90	95	—
6	120	140	+20	120	70	-50	30	YES	normal	2100	1900	100	90	—
7	125	150	+25	125	70	-55	30	YES	normal	2300	2400	90	95	40
8	110	120	+10	110	65	-45	30	NO	—	—	—	—	—	35
9	120	130	+10	120	50	-70	30	YES	normal	1800	2100	90	90	30
10	100	110	+10	100	80	-20	30	YES	normal	2200	1900	85	90	35
AVERAGE	118	133	+15	118	63	-55								

Fig. 2.—*Descending thoracic aortic bypass employing a left auricle to femoral artery shunt with gravity return from the left auricle.* This system is similar to that shown in Fig. 1, but blood is syphoned rather than pumped from the left auricle. At moderate flow rates it is possible to decompress the proximal aorta, adequately perfuse the distal viscera, and obtain a high rate of survival after 90-minute shuntings.

and, in practice, would stress the system less and involve less pumping trauma to the blood. A flow of 30 c.c./Kg./min. may be a reasonable minimum, resulting in a proximal pressure rise of about 16 mm. Hg and distal drop of 55 mm. Hg to a mean of 65 mm. Hg. At flow below this level, not only does the distal pressure drop to precariously low levels, but the proximal pressure rises to dangerously high values. At flows much in excess of 75 c.c./Kg./min. the demand of the pump exceeds the flow into the auricle, and the tubing on the inflow side of the pump collapses. Four consecutive dog subjects were shunted for 90 minutes at the previously stated minimum flow rate of 30 c.c./Kg./min. Survival of the animals was attempted to evaluate adequacy of visceral perfusion under these circumstances. All dogs survived and showed no evidence of injury at 1 week. Hemoglobin concentrations at the end of the 90-minute run in these dogs were approximately 35 mg. per cent.

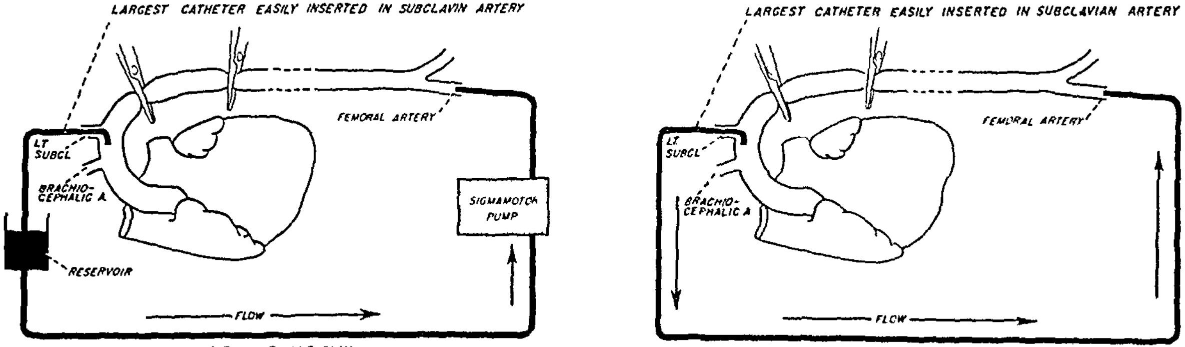
2. *Left auricle to femoral artery shunt with gravity return from the left auricle:* This apparatus is shown in Fig. 2. Here a collecting inflow reservoir is intrinsic in the apparatus. A greater priming volume is required, and flow rates are determined and limited by the size of tubing used and hydrostatic pressure head available in the syphon. Flows are thus determined by purely hydraulic considerations and can be predicted by reference to Fig. 9, which shows the relation of flow rate to inflow tubing size and pressure head. With the apparatus used, the maximum flows obtainable ranged from 60 to 70 c.c./Kg./min. in the 6 dogs run. Ninety-minute shuntings at the previously stated minimum flow of 30 c.c./Kg./min. were made in 6 dogs. Five dogs showed no evidence of injury at the end of 1 week. One dog died of hemothorax and massive atelectasis at the end of 4 hours.

3. *Simple subclavian artery to femoral artery shunt without pump return from the subclavian artery:* The apparatus used is shown in Fig. 3. In 3 dogs, the subclavian catheter was allowed to bleed into a collecting reservoir in order that flows could be measured by means of the calibrated pump. These flows were below the previously defined minimum of 30 c.c./Kg./min. and could only have been lower had the simple subclavian artery to femoral artery shunt, which the apparatus was intended to simulate, been used. Two additional dogs were run using the simple shunt, and pressure levels were comparable.

Of these 5 dogs, 4 survived, 1 dying of hemorrhage a few hours after the experiment. Of these 4 surviving dogs, 2 were in good condition at the end of 1 week and 2 showed evidence of renal injury.

This limitation of flow is obviously due to the small caliber of the arterial catheters and the limited pressure available in the proximal aorta, and could be avoided by subclavian or aortic cannulation using larger tubing. However, the relative simplicity and ease of inserting small subclavian and femoral artery catheters make this a desirable shunting circuit past descending aortic lesions, if flows could be made adequate.

4. *Subclavian to femoral artery shunt with pump return from the subclavian artery:* The arrangement shown in Fig. 4 was used in an effort to overcome the insufficient flows of the simple subclavian artery to femoral artery



SIMPLE SHUNT PLUS PUMP (DOGS • 13,14,15)

SIMPLE SHUNT (DOGS • 16 17)

DESCENDING THORACIC AORTIC BYPASS

SUBCLAVIAN TO FEMORAL ARTERY SHUNT WITHOUT PUMP RETURN FROM SUBCLAVIAN

MEAN PRESSURE (mm/Hg) DATA, SHUNT FLOW AND SURVIVAL RESULTS FOR NINETY MINUTE DESCENDING AORTIC BYPASS

DOG NO.	MEAN PRESSURE IN PROX AORTA BEFORE BYPASS	MEAN PRESSURE IN PROX AORTA DURING BYPASS	MEAN PRESSURE CHANGE IN PROX AORTA	MEAN PRESSURE IN DISTAL AORTA BEFORE BYPASS	MEAN PRESSURE IN DISTAL AORTA DURING BYPASS	MEAN PRESSURE CHANGE IN DISTAL AORTA	FLOW IN SHUNT cc/Kg/min	SURVIVALS	COMPLICATIONS					HEMOGLOBIN CONC. AT NINETY MIN. (mg %)
									NEUROLOGICAL	UROLOGICAL				
										CONC POWER (mosm/L)		CREAT CLEARANCE (cc/min)		
										PRE-OP	POST OP	PRE-OP	POST-OP	
13	120	150	+30	120	40	-80	25	NO	normal	—	—	—	—	—
14	110	140	+30	110	40	-70	20	YES	normal	2000	1900	90	95	40
15	110	145	+35	110	35	-75	15	YES	normal	2100	*1600	90	* 60	—
16	120	150	+30	120	30	-90	unknown	YES	normal	2200	*1380	85	* 55	—
17	130	160	+30	130	35	-95	unknown	YES	normal	2400	2200	90	100	20
AVERAGE	118	149	+31	118	35	-82								

* ABNORMAL RENAL FUNCTION

Fig. 3.—*Descending thoracic aortic bypass employing a subclavian to femoral artery shunt without pump return from the subclavian.* Here the subject's arterial pressure provides the impetus for shunt flow. This system gives only marginal flow rates and results in high proximal pressures and, on occasion, inadequate distal perfusion.

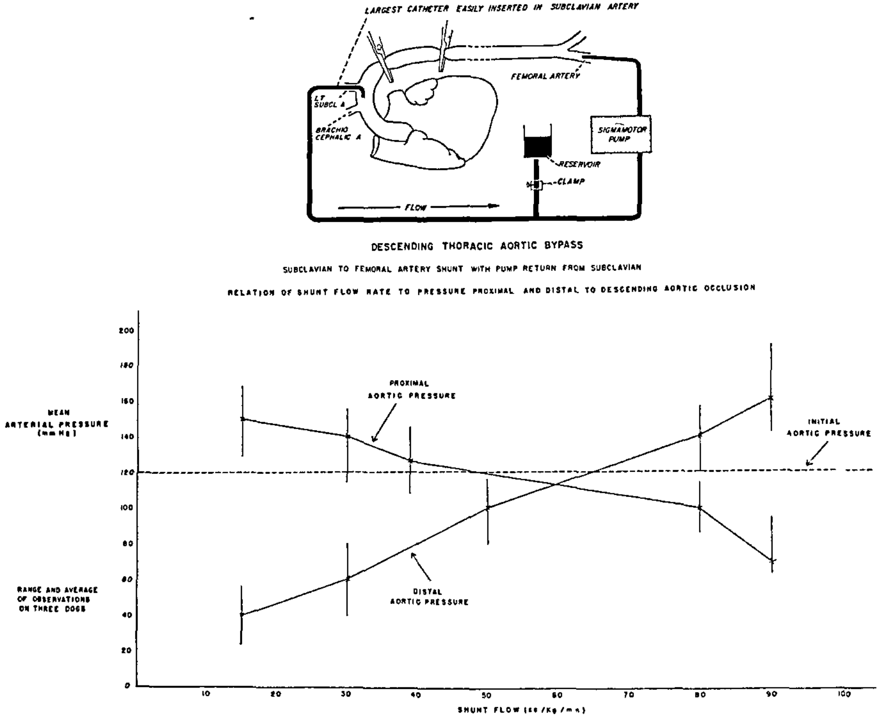


Fig. 4 —*Descending thoracic aortic bypass employing a subclavian to femoral artery shunt with pump return from the subclavian artery.* The subject's arterial pressure is complemented by a pump to provide a greater impetus to shunt flow. It is possible to obtain physiologic flows and essentially normal pressures, proximal and distal to the aortic occlusion, by this method.

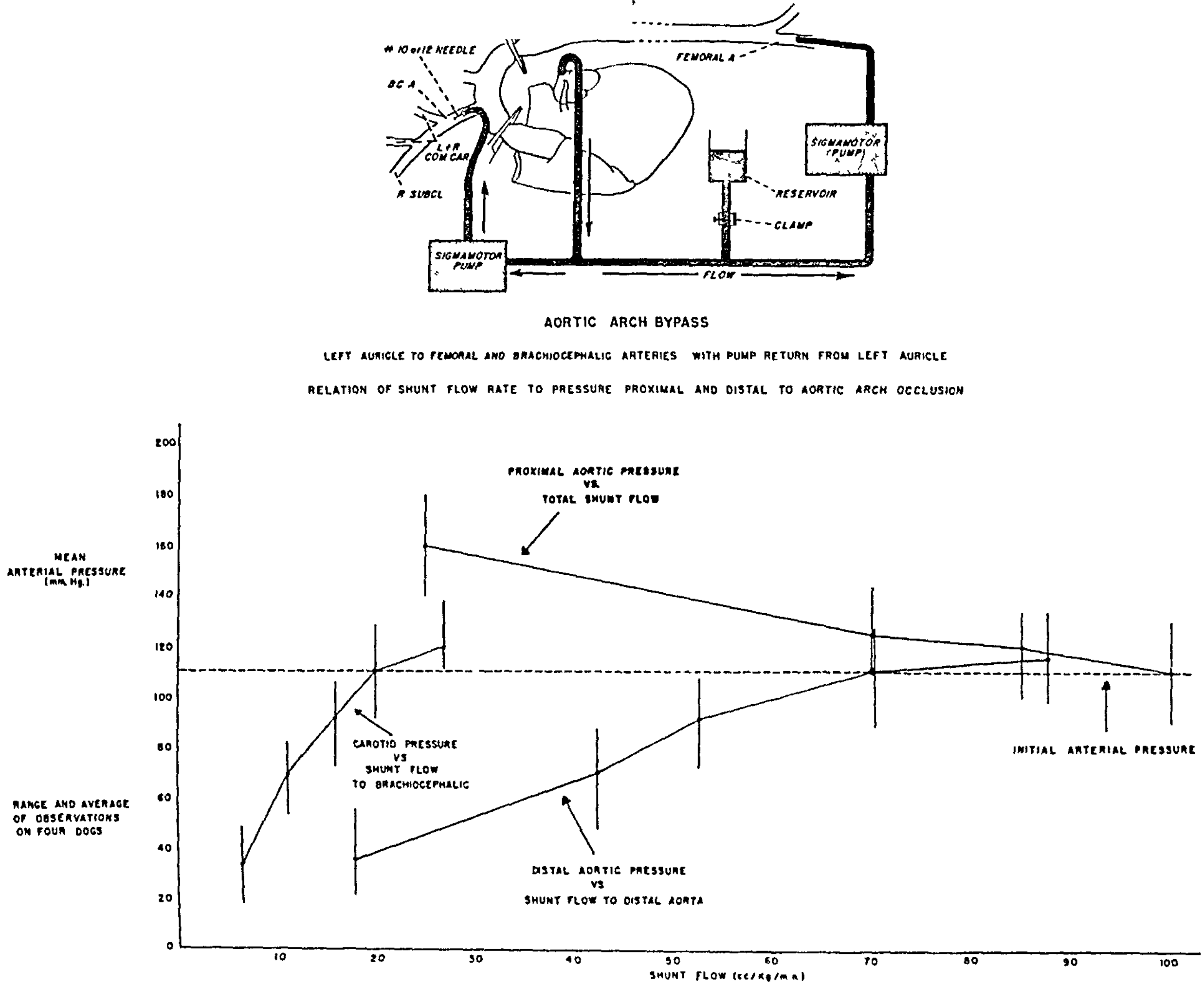


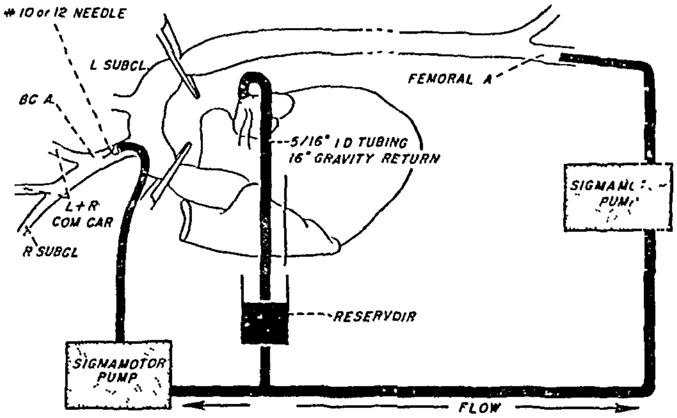
Fig. 5.—*Aortic arch bypass employing a left auricle to femoral and brachiocephalic arteries shunt with pump return from the left auricle.* Oxygenated blood is removed by active suction from the left auricle and supplies the distal visceral structures and cerebrum via the femoral and brachiocephalic arteries, respectively. The residual left auricular blood passes through the left ventricle and supplies the coronary vessels. It is possible to obtain physiologic flows and essentially normal pressures, proximal and distal to the aortic occlusion, by this method.

shunt by the interposition of a pump Five dogs were run, 3, in order to explore possible flows, and the last 2 to test survival with the 30 c c /Kg /min flow The effect of various flows on proximal and distal aortic pressure corresponds with the data obtained from the similar study with left auricle to femoral artery shunt It is quite possible to obtain high flows in the dog in this manner Two surviving dogs showed no ill effects at 1 week

Arch of Aorta Bypass—

Two shunting arrangements were tested (1) active pumping from the left auricle to the femoral artery and the brachiocephalic artery with the application of suction to the left auricle, and (2) gravity flow from the left auricle to a reservoir, thence pumping to the femoral artery and brachiocephalic artery

1 *Left auricle to femoral and brachiocephalic arteries with pump return from left auricle* This apparatus is shown in Fig 5 An additional pump is used in this system to supply the brachiocephalic artery and thence both carotids and the right vertebral artery A No 10 or 12 needle is used in the dog subjects to perfuse the brachiocephalic artery because this is large enough for the flow required but not so large as to occlude completely the artery at a time when the extracorporeal circuit is not in use Fig 5 shows the effect of varying flow rate on mean arterial pressure, proximal and distal (aorta and carotid) to the point of aortic occlusion It will be noted that these three pressures are equal and also approximate the aortic pressure before occlusion at a flow of about 100 c c /Kg /min (20 to 25 c c /Kg /min to the head and 70 to 75 c c /Kg /min to the rest of the subject) Once again flows less than this ideal are allowable and probably desirable Sixty cubic centimeters per kilogram per minute (15 c c /Kg /min to the head and 45 c c /Kg /min to the rest of the subject) may be a reasonable minimum, resulting in a proximal pressure rise of 26 mm Hg and a distal pressure drop in the carotids and aorta of 40 mm Hg to a pressure of 70 mm Hg At flows below this level not only did the distal pressures drop to precariously low levels but the proximal aortic pressure rose to dangerously high values, at flows below 40 c c /Kg /min, evidence of left ventricular strain occurred, cardiac action became irregular, and cardiac arrest or ventricular fibrillation ensued within 5 minutes in almost every case Even at 60 c c /Kg /min, cardiac irregularities sometimes occurred in the initial period after aortic occlusion, but these signs usually disappeared within 10 minutes, if the catheter was correctly positioned to obtain adequate outflow On occasion it was necessary to place the catheter through the mitral valve In all cases of proximal aortic occlusion it was essential to make multiple vents in the catheter to avoid outflow obstruction At flows much in excess of 100 c c /Kg /min, the demand of the pump exceeded the flow into the auricle and the tubing on the inflow side of the pump would collapse Ninety minute shuntings at the previously stated minimum flows of 60 c c /Kg /min were made in 2 dogs and survivals were attempted in order to evaluate adequacy of this type



AORTIC ARCH BYPASS

LEFT AURICLE TO FEMORAL AND BRACHIOCEPHALIC ARTERIES

WITH GRAVITY RETURN FROM LEFT AURICLE

MEAN PRESSURE (mm.Hg) DATA, SHUNT FLOW AND SURVIVAL RESULTS FOR NINETY MINUTE AORTIC ARCH BYPASS

DOG NO	MEAN PRESSURE IN PROXIMAL AORTA		MEAN PRESSURE CHANGE IN PROXIMAL AORTA	MEAN PRESSURE IN DISTAL AORTA		MEAN PRESSURE CHANGE IN DISTAL AORTA	MEAN PRESSURE IN CAROTID ARTERY		MEAN PRESSURE CHANGE IN CAROTID ARTERY	SHUNT FLOW cc./Kg./min		SURVIVALS	COMPLICATIONS					Hgb CONC AT NINETY MINUTES
													NEURO	UROLOGICAL				
														CONC. POWER (mosm./L)		CREAT. CLEAR. (cc./min)		
	BEFORE BYPASS	DURING BYPASS		BEFORE BYPASS	DURING BYPASS		BEFORE BYPASS	DURING BYPASS		FEM-ORAL	BRACHIO-CEPHALIC			PRE-OP	POST-OP	PRE-OP	POST-OP	mg.%
27	100	120	+20	100	55	-45	100	80	-20	42	18	YES	normal	2000	2100	90	90	70
28	110	120	+20	110	70	-40	110	75	-35	42	18	NO	—	—	—	—	—	—
29	120	135	+15	120	60	-60	120	60	-60	42	18	YES	normal	2200	2400	80	90	65
30	110	140	+30	110	80	-30	110	65	-45	42	18	YES	normal	2400	2000	90	80	—
AVERAGE	110	131	+21	110	66	-44	110	70	-40									

Fig. 6.—*Aortic arch bypass employing a left auricle to femoral and brachiocephalic arteries shunt with gravity return from the left auricle.* This system is similar to that shown in Fig. 5 except that oxygenated blood is syphoned rather than pumped from the left auricle. At moderate flow rates it is possible to decompress the proximal aorta, adequately perfuse the distal visceral and cerebrum, and obtain a high rate of survival after 90-minute shuntings.

of perfusion under these circumstances. Both dogs showed no evidence of injury at the end of 1 week. Hemoglobin concentration in the plasma at the end of the 90-minute perfusions was approximately 70 mg. per cent.

2. *Left auricle to femoral artery and brachiocephalic artery with gravity return from the left auricle:* This apparatus is shown in Fig. 6. With the apparatus used, the maximum flows obtainable ranged from 60 to 70 c.c./Kg./min. With gravity return when the ascending aorta is occluded, it is particularly important to have the catheter correctly positioned for adequate outflow; on occasion, cannulation of the mitral valve was necessary. Ninety-minute shuntings at the previously stated minimum flows of 60 c.c./Kg./min. were made in 4 dogs. Three dogs showed no evidence of injury at the end of 1 week. One dog died of hemothorax and massive atelectasis at 12 hours postoperatively.

Ascending Aortic Bypass.—

Two shunting arrangements were tested: (1) active pumping from the left auricle to the femoral artery with application of suction to the left auricle, and (2) gravity flow from the left auricle to a reservoir, thence pumping to the femoral artery.

1. *The left auricle to femoral artery shunt with pump return from the left auricle:* This apparatus is shown in Fig. 7. Once again the effect of varying flow rate on mean arterial pressure proximal and distal to the point of aortic occlusion was studied. It will be noted in Fig. 7 that, at a flow of 100 c.c./Kg./min., these two pressures were approximately equal and also approximated the aortic pressure before occlusion. A flow of about 60 c.c./Kg./min., which may be a reasonable minimum, resulted in a mean proximal pressure rise of 30 mm. Hg and a distal pressure fall of 50 mm. Hg, to a level of 70 mm. Hg. At flows below this level the distal pressure dropped to precariously low levels and the proximal pressure rose to dangerously high values. In all cases, at flows below 30 to 40 c.c./Kg./min. there was electrocardiographic evidence of severe left heart strain, and cardiac arrest or ventricular fibrillation almost always occurred within 5 minutes. At 60 c.c./Kg./min., transitory cardiac irregularities were again noted. At flows much in excess of 100 c.c./Kg./min. the demand of the pump exceeded the flow into the auricle and the tubing on the inflow side of the pump collapsed. Ninety-minute shuntings at the previously stated minimum flow rate of 60 c.c./Kg./min. were made and survival was attempted in 3 dogs. Two of the 3 dogs survived and were well at the end of 1 week. One died of unknown cause at 24 hours.

2. *Left auricle to femoral artery with gravity return from the auricle:* The apparatus is shown in Fig. 8. Actual flows obtainable by this system ranged from 60 to 70 c.c./Kg./min. in the 5 dogs run. Ninety-minute shuntings at the previously stated minimum flows of 60 c.c./Kg./min. were made and survival of the animals was attempted. Four of the 5 dogs survived and showed no evidence of injury at the end of 1 week. One dog died 6 hours postoperatively from massive atelectasis.

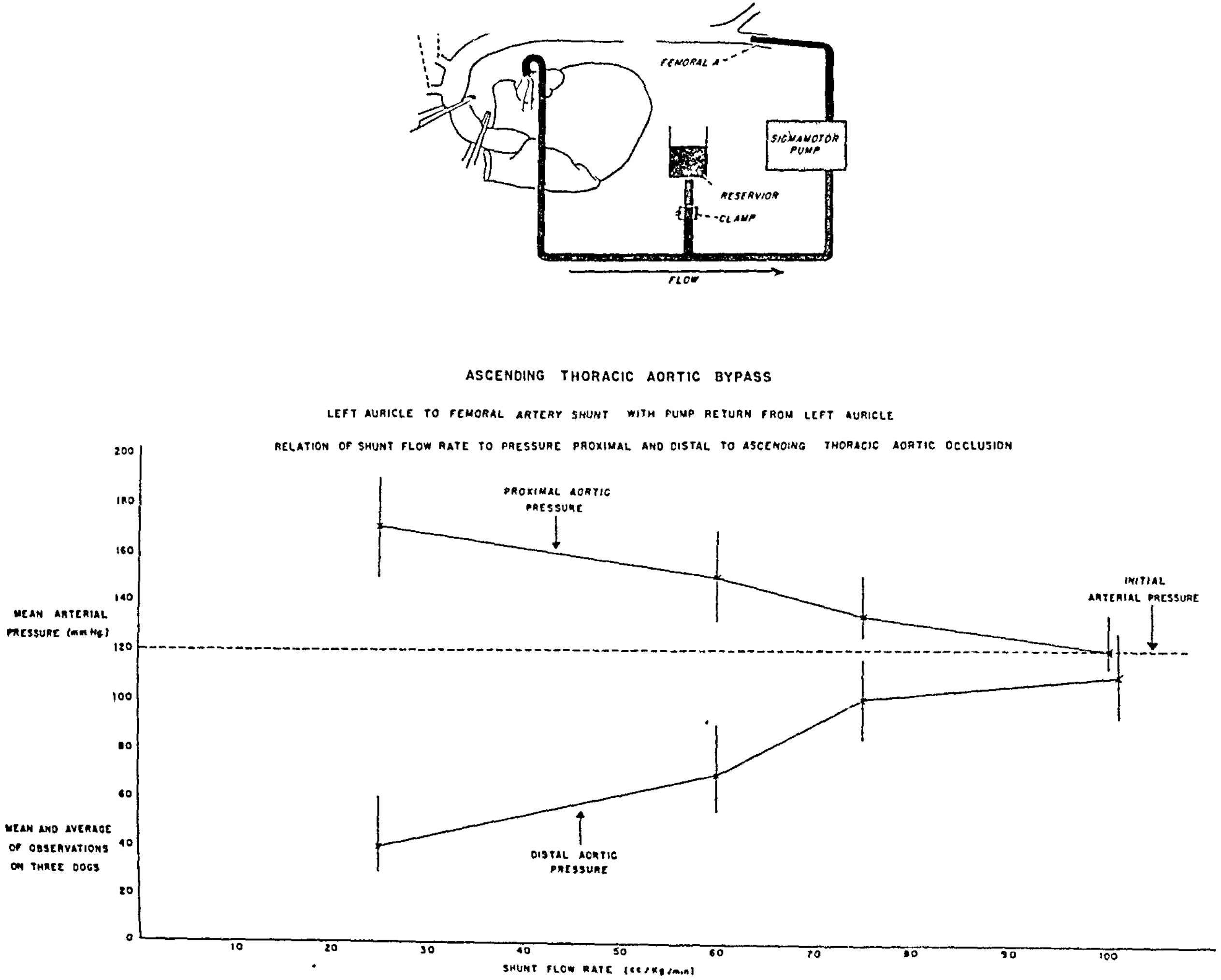
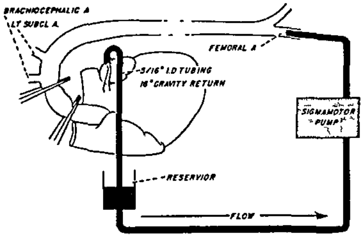


Fig. 7.—*Ascending thoracic aortic bypass employing a left auricle to femoral artery shunt with pump return from the left auricle.* By this system oxygenated blood is removed by active suction from the left auricle and via the femoral artery perfuses all aortic branches except the coronaries. The residual left auricular blood passes through the left ventricle and supplies the coronary vessels. It is possible to obtain physiologic flows and essentially normal pressures, proximal and distal to the aortic occlusion, by this method.



ASCENDING THORACIC AORTIC BYPASS

LEFT AURICLE TO FEMORAL ARTERY SHUNT WITH GRAVITY RETURN FROM LEFT AURICLE

MEAN PRESSURE (mmHg) DATA SHUNT FLOW AND SURVIVAL RESULTS FOR NINETY MINUTE ASCENDING THORACIC AORTIC BYPASS WITH AND WITHOUT CARDIAC ARREST

DOG NO.	MEAN PRESSURE IN PROX. AORTA BEFORE BYPASS	MEAN PRESSURE IN PROX AORTA DURING BYPASS	MEAN PRESSURE CHANGE IN PROX. AORTA	MEAN PRESSURE IN DISTAL AORTA BEFORE BYPASS	MEAN PRESSURE IN DISTAL AORTA DURING BYPASS	MEAN PRESSURE CHANGE IN DISTAL AORTA	FLOW IN SHUNT cc/Kg/min.	SURVIVALS	COMPLICATIONS					HEMOGLOBIN CONC AT NINETY MIN. mg %
									NEUROLOGICAL	UROLOGICAL				
										CONC. POWER (mosm./L) PRE OP.	POST OP.	CREAT CLEARANCE cc/min. PRE OP.	POST OP.	
	WITHOUT CARDIAC ARREST													
34	120	145	+25	120	80	-40	80	NO	—	—	—	—	—	—
35	130	150	+20	130	60	-70	60	YES	normal	2000	1900	90	95	70
36	110	140	+30	110	55	-55	60	YES	normal	2300	2400	100	85	75
37	100	130	+30	100	75	-25	60	YES	normal	1800	2000	90	95	—
38	110	120	+10	110	60	-50	60	YES	normal	—	—	—	—	—
AVERAGE	114	137	+23	114	66	-48								
	WITH CARDIAC ARREST													
39	120	10	-110	120	80	-40	60	YES	normal	2200	2100	85	90	—
40	130	15	-115	130	70	-50	60	NO	—	—	—	—	—	—
41	130	15	-115	130	70	-60	80	NO	—	—	—	—	—	—
ERAGE	127	13	-114	127	73	-50								

Fig 8—*Ascending thoracic aortic bypass employing a left auricle to femoral artery shunt with gravity return from the left auricle* This system is similar to that shown in Fig. 7 but syphons rather than pumps blood from the left auricle At moderate flow rates it is possible to decompress the proximal aorta adequately perfuse the distal viscera, and obtain a high rate of survival after 90-minute shuntings Even in the presence of cardiac arrest, passive flow of blood through the lungs provides sufficient blood for adequate flows

In our investigation of the ascending aorta, an interesting phenomenon was noted. We could consistently clamp off the aorta up to approximately 2.5 cm. from the coronary ostia without any cardiac difficulty as long as appropriate flows were maintained, but occlusion closer than 2.5 cm. invariably caused cardiac arrest. Simultaneous pressure and electrocardiographic studies suggested that this phenomenon was due to myocardial ischemia.

The elastic reservoir in such a shortened aortic segment is too small to store during systole and deliver during diastole a sufficient volume of coronary flow. Heart action could be maintained by introducing additional blood into this segment from the pump, unless the clamp was so close to the heart as to occlude the coronary arteries. Three dogs were studied with the proximal clamp less than 2.5 cm. from the coronary ostia. Cardiac arrest occurred within 5 minutes in each case, but, in spite of arrest, after administration of transfusions to increase venous pressure, blood flow from the left auricle continued and was comparable in amount to that obtained without arrest. As shown in Fig. 8, these 3 dogs, which were perfused for 90 minutes at a flow of 60 c.c./Kg./min., had similar distal pressure studies as those obtained from the previous dogs which had normal cardiac action. Of course the proximal aortic pressure was low because of the absence of cardiac action. Two of these 3 dogs were readily resuscitated after the perfusion by removal of the clamp and defibrillation. One of the dogs was living and well at 1 week; the other died of a cardiac arrhythmia at 5 hours postoperatively. We were unable to resuscitate the heart of the third dog.

CASE REPORTS

The following pertinent clinical cases are reported and considered in the light of this animal work.

CASE 1.—C. J. (M.G.H.—Unit No. 108670) was a 60-year-old man who entered the hospital with a syphilitic thoracic aortic aneurysm, symptomatic for 10 years with recent onset of substernal pain radiating to the back. He had had a myocardial infarction 6 years prior to admission and had hypertension of 190/120 mm. Hg, but his heart was of normal size without evidence of valvular disease. According to an angiocardiogram, the aneurysm lay in the upper descending aorta just beyond the left subclavian artery.

At operation, the aneurysm was resected and replaced by an aortic homograft, using a left heart bypass from left auricle to femoral artery. Blood was taken via a gravity system from the left auricle through a tube, 0.8 cm. I.D., to a reservoir, thence pumped into the femoral artery through a No. 20 catheter.

The aneurysm ruptured during the procedure while it was being freed up prior to control of the aorta. The resultant massive hemorrhage and cardiac arrest were controlled by starting the bypass system and clamping the aorta proximal and distal to the lesion. The heart was readily resuscitated with intermittent compression and replacement of blood loss through the reservoir. Resection and graft required a left heart bypass of 1 hour and 20 minutes. During the first hour of bypass, the gravity return syphon was maintained at 18 inches and gave a perfusion flow of 1,500 c.c./min. (20 c.c./Kg./min.) and a proximal aortic pressure 30 mm. Hg above normal. During the last 20 minutes of perfusion, the gravity return syphon was increased to 25 inches with a resultant rise in perfusion flow to 2,250 c.c./min. (30 c.c./Kg./min.) and a resultant decrease in proximal pressure to only

14 mm Hg above normal As can be seen in Fig 9, for an inflow tube, 0 8 cm I D, the above pressure differentials and resultant flows could be predicted from our previous in vitro data

Postoperatively, the patient had a moderately severe oliguria for 3 days, but was eventually discharged without evidence of renal or neurological deficit and was well when last seen 9 months after operation

Comment The tubing size and original height of syphon in this case limited shunt flow to marginally adequate levels, resulting in elevation of the proximal aortic pressure during operation and temporary postoperative renal dysfunction

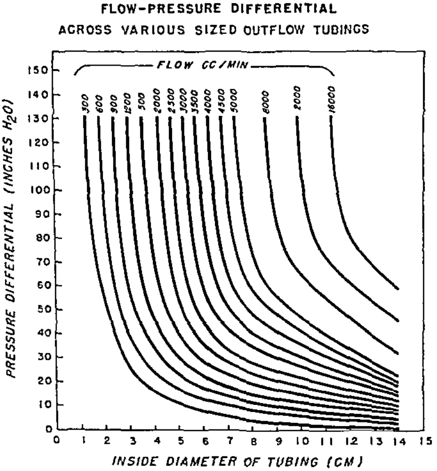


Fig 9—*Flow pressure differential relationship of various sized outflow catheters* The amount of pressure differential across various sized outflow catheters (12 inches in length) necessary to obtain a given flow is inversely proportional to the square of the inside diameter of the catheter

It would have been desirable to have either larger tubing from the left auricle, or, as was eventually done, a stronger suction to provide a larger shunt

The availability of reservoir prime in the bypass system, and suction apparatus to return blood from the operative field to the system readily solved an otherwise irretrievable situation with rupture of the aneurysm

CASE 2—J F (M G H—Unit No 1002417), a 63 year old known hypertensive man with a previous history of myocardial infarction, entered the hospital with acute pain in the interscapular and substernal regions radiating down the left arm Thirty hours after admission a diagnosis of dissecting aneurysm was made on the basis of x ray findings and the sudden development of paraplegia

At surgery, fenestration of the aneurysm in the descending aorta was performed, using a simple shunt from the left subclavian to the femoral artery with No 18 catheters to bypass the occluded segment of descending aorta The aorta was occluded for 40 minutes Distal arterial pressures were not measured but could be expected to be low since the proximal aortic pressure was not well decompressed by the shunt alone, and required administration of Arfonad during occlusion to keep it near pre-occlusion levels. There was severe oliguria for 4 days after operation (with good recovery of renal function and slight recovery from paraplegia at the time of discharge, 60 days after operation).

Comment: The simplicity of a simple shunt argues in its favor, but again flows to the lower body were hardly adequate as evidenced by the postoperative depression of renal function.

Because of the narrow caliber of the arterial catheters, required flows will be limited and the pressure differential between the two systems will be high. The interposition of a pump in such a shunt will improve flow and lower proximal arterial pressure as shown by the animal experiments.

Case 3.—A. P. (M.G.H.—Unit No. 917634), a 64-year-old man, had had a known symptomatic syphilitic ascending aortic aneurysm for 2½ years. During the week prior to admission there had been sudden increase in right anterior chest pain and an appreciable increase in the size of the aneurysm. He was in mild congestive failure at the time of admission.

At operation, the apparent recent increase in aneurysmal size was found to be due to rupture of the right lateral wall of the ascending aortic aneurysm. Open reconstructive aneurysmorrhaphy was performed, using a left heart bypass consisting of a two tube (0.8 cm. I.D.), 25-inch syphon from the left auricle to a reservoir from which blood was pumped into the femoral artery through a No. 20 catheter.

Twelve minutes were required for evacuation of thrombus from the aneurysm, mobilization of relatively healthy vessel wall, and the application of a long clamp to restore aortic continuity. During this period, the aorta was clamped about 1 cm. beyond the aortic valve and at the innominate artery, and cardiac action gradually weakened and finally ceased, due to interference with coronary circulation by the proximal clamp. When aortic continuity had been restored, the clamps were removed and the left heart bypass was continued over the next 18 minutes, during which time strong cardiac action gradually returned.

A flow rate of approximately 4,000 c.c./min. (60 c.c./Kg./min.) with a resulting mean distal arterial pressure of from 80 to 90 mm. Hg was maintained during bypass, both before and during cardiac arrest. This is consistent with the experimental data shown in Fig. 9 for two tubings, 0.8 cm. I.D., with a 25-inch pressure differential. Postoperatively, the patient had a mild and transient oliguria for the first 24 hours without evidence of serious renal injury. His course was complicated by the development of auricular fibrillation and congestive failure. He also showed marked respiratory insufficiency attributable to the fact that both phrenic nerves had been cut during dissection of the aneurysm. He required the assistance of a respirator for 25 days. Thirty days after operation, the patient was ambulatory, breathing well, and asymptomatic when he suddenly died. Autopsy showed sepsis at the aortic suture line with resultant rupture and exsanguination.

Comment: The shunt flow of 60 c.c./Kg./min. past the obstructed ascending aorta provided adequate body perfusion in this case. Resistance to flow in the syphon tubing because of its greater size was considerably less than in Case 1, thus permitting the greater flow. Placement of the proximal aortic clamp too close to the coronary ostia resulted in cardiac arrest, but passive flow of blood through the lungs was sufficient to maintain perfusion and provide aortic pressure sufficient to resuscitate the heart.

Case 4.—C. H. (M.G.H.—Unit No. 1008693), a 50-year-old man known to be hypertensive, was admitted with a dissecting aneurysm of the thoracic aorta of 40 hours' duration.

During the first few hours of hospitalization, he developed progressively severe symptoms of cardiac tamponade so an attempt to repair the primary tear in the ascending aorta was made At operation, 400 c c of blood was released from the pericardium and a left auricle to femoral artery bypass was set up, using an inflow tube, 1 4 cm I D, with a 21 inch syphon from the left auricle Blood was returned by a Sigmamotor pump through a No 20 catheter in the femoral artery The aorta was clamped at the innominate artery, 2 5 cm from the heart A shunt flow of 4,500 c c /min (70 c c /Kg /min) was obtained which resulted in a mean distal arterial pressure of 100 mm Hg as compared with a mean pressure before clamping of 150 mm Hg This flow is consistent with the experimental data shown in Fig 9 for a 1 4 cm I D tubing with 21 inch syphon pressure differential

During the first 10 minutes of perfusion, an attempt was made to identify and repair the primary tear This was abandoned when the aorta tore free from the heart just beyond the coronary orifices proximal to the controlling clamp With no effective coronary perfusion, cardiac action ceased Nevertheless body perfusion continued at the previous level employing the left auricle to femoral artery shunt While bleeding from the left ventricle was minimized by pressure on the outflow tract, an aortic homograft was obtained and sutured end to end to replace the ascending aorta Following restoration of aortic continuity, the ventricle was observed to be fibrillating and electrical defibrillation was accomplished The left heart bypass was continued in parallel with the patient's own heart for about 5 minutes, following which time the shunt was discontinued and the patient was able to maintain a blood pressure at 140/80 mm Hg A shunt flow of 70 c c /Kg /min was maintained throughout the 1½ hour bypass the blood moving passively through the lungs during the 1 hour and 20 minutes of cardiac arrest

Postoperative electrocardiogram was unchanged from that observed preoperatively Vital signs were well maintained and the patient had recovered consciousness when, about 4 hours after operation in the recovery room there was a rush of blood from the left chest drainage tube and the patient died Autopsy permission was not obtained

Comment The left heart bypass was adequate in this case requiring prolonged ascending aortic occlusion Flows sufficient to maintain a satisfactory arterial pressure could be obtained with a syphon of adequate caliber and height from the left auricle However, a pump return system would have been simpler and would have avoided the inconvenience of a large inflow tube and syphon gradient Even with cardiac arrest, this system maintained adequate perfusion flow and pressures

DISCUSSION

Left heart bypass offers a relatively simple means of compensating for thoracic aortic occlusion Since no oxygenator is necessary, the required tubing and fittings can be stored sterile and assembled for prompt use in the operating room The apparatus requires less than 500 c c of blood or saline for priming, minimizes the problem of air embolization, and avoids the current uncertainties of a pump oxygenator in long perfusion With its reservoir, this system gives an excellent safeguard against massive hemorrhage and enables immediate transfusion or autotransfusion

This type of bypass can be employed in any of the three thoracic areas—ascending aorta, arch, or descending thoracic aorta When correct shunt flows are maintained, it is possible to perfuse distal structures adequately and to avoid proximal hypertension and left heart strain Proximal hypertension and cardiac arrhythmias become a problem and spinal cord and renal damage may occur when flows are too low. Unnecessarily high flows will only put an added burden on the pumping apparatus and increase blood element damage.

For lesions involving only the descending thoracic aorta, either the left auricle or the subclavian artery is an equally good source of blood for shunting. The source most readily available in the operative field should be used. If the left auricle is used, either active pumping or gravity return from the left auricle can be employed. In order to obtain adequate flow with gravity, a large catheter must be used and an adequate syphon assured (Fig. 9). Pump suction allows the use of a smaller auricular catheter and eliminates concern about the height of the syphon. If the subclavian artery inflow system is employed it is almost mandatory to use a pumping system for long occlusions because a simple shunt with small easily insertable catheters is unable to transmit more than marginal flows.

For shunts past lesions of the ascending aorta or aortic arch, the left auricle is the only logical source of inflow blood. Here again, either active pumping or gravity return can theoretically be employed, but the increased flow requirement emphasizes the advantages of the pump return (Fig. 9). The dangers of inadequate flow are most apparent in ascending aortic occlusion, where low flows will result in severe proximal hypertension, left heart strain, and cardiac difficulties.

When occlusion occurs very close to the aortic valve, cardiac arrest may occur from insufficient coronary perfusion. This may result either from occlusion of the coronary ostia or as a result of there being inadequate systolic blood volume in the proximal aortic segment to fill the vessels during diastole. This difficulty was overcome here, as by Johnson,[9] by introducing blood from the pump into the proximal aortic segment.[9] As shown in dog experiments[10] and demonstrated in Case 9, even where cardiac arrest has occurred, the pressure of peripheral venous blood, when elevated by transfusion, circulates sufficient blood through the lungs and the left auricle to allow adequate pump flows with resultant satisfactory distal perfusion flow and pressure for periods of time up to 1 hour. Such an arrangement imposes the temporal limitations of ischemic cardiac arrest, and prolonged procedures would require cardiac cooling or some method of coronary perfusion.

CONCLUSIONS

1. Simple shunting around the occluded segment using a pump but not employing an oxygenator promises to be a feasible method of handling aneurysms in all areas of the thoracic aorta. (a) A simple circuit consisting of a pump from the auricle to the distal arterial tree with a reservoir attached to the intake line allows the most satisfactory control of flow rates and pressures. (b) In the case of the descending aorta, the subclavian artery can be substituted for the left auricle as a source of oxygenated blood, but adequate control of flow rate still requires a pump return system.

2. By simple regulations, the shunt flow and pressure in all areas can be controlled. Normal pressures and flows, both proximal and distal to the area

of occlusion, can be obtained but considerably less than normal pressures and flows are acceptable and compatible with recovery In the dog, ideal and minimal acceptable flow rates at the various levels of aortic obstruction are shown in Table I

TABLE I

	IDEAL (C C /KG /MIN)	MINIMAL ACCEPTABLE (C C /KG /MIN)
Descending aorta	75	30
Aortic arch		
Distal aorta	70 to 75	45
Thoracocervical trunk	20 to 25	15
Ascending aorta	100	60

Survival studies employing minimal acceptable flow rates at these three levels are shown in Table II

TABLE II SURVIVAL RESULTS OF 90 MINUTE SHUNTINGS AROUND ISOLATED SEGMENTS OF THORACIC AORTA

AREA	NO OF DOGS	SURVIVALS	% SURVIVALS
Descending thoracic aorta	17	15	88
Aortic arch	6	5	83
Ascending thoracic aorta	11	7	64

3 Even in the face of cardiac arrest, these shunting systems can, as a temporary expedient, provide adequate flow and pressure during occlusion of the ascending aorta or aortic arch

SUMMARY

In dealing with aneurysms or acute lesions of the thoracic aorta, it is necessary to shunt blood past any temporarily occluded segment, in order to perfuse the distal structures as well as to avoid proximal hypertension and left heart strain

Temporary occlusion with bypass of the ascending aorta, the aortic arch, and the descending aorta were considered separately in these dog experiments Various shunting arrangements were tried for each level of occlusion and the method most applicable for clinical use determined For each shunting arrangement, measurement of flow rates and their relationship to proximal and distal pressure was accomplished Optimal and minimally acceptable flow rates were determined by pressure studies and by animal survival of 90 minute occlusions of the thoracic aorta without central nervous system or visceral injury Pertinent clinical cases are presented and discussed

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REPAIR OF MITRAL INSUFFICIENCY DUE TO RUPTURED CHORDAE TENDINEAE

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That insufficiency of the mitral valve is correctable by open heart surgery has been amply demonstrated. The surgical technique has been based on the assumption that pure mitral insufficiency is the result of an absolute or relative deficiency of valve leaflet tissue in relation to the size of the mitral orifice. Thus, surgical correction has been accomplished either by narrowing the mitral annulus or by replacing deficient valvular tissue with immobile occluding prosthetic elements.[1-5] No different specific technique has been described for the correction of mitral insufficiency in the circumstance where it results from rupture of the chordae tendineae. The purpose of this communication is to illustrate a technique for the repair of such lesions and point out that, in certain instances, reconstruction of a competent mitral valve can be accomplished without mitral annuloplasty and without the use of prosthetic materials.

The chordae tendineae are crucially important to the normal function of the mitral valve, for they prevent eversion of its leaflets into the left atrium during ventricular systole.[6] Rupture of one or more chordae tendineae is occasionally the mechanism whereby mitral insufficiency results from rheumatic or bacterial endocarditis and also may result from external trauma.[7]

SURGICAL TECHNIQUE

Access to the operative area is achieved by right anterolateral thoracotomy in the bed of the intact sixth rib. Extracorporeal circulation[8] is instituted after cannulation of the venae cavae via the right atrial appendage and of the right external iliac or common femoral artery. The left atrium is widely incised just posterior to the interatrial sulcus. A sucker is inserted into the heart and the large amount of central blood is withdrawn. Just enough blood is left in the heart to cover the mitral orifice. Cardiac asystole is not instituted, because ventricular action is required so that the surgeon can assess the function of the valve and ascertain the area from which regurgitation originates. Thus, any systolic eversion of a portion of leaflet devoid of chordal attachment can be detected, as well as the regurgitant jet originating at the same area (Fig. 1, *a*).

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After an estimate has been made of the length of the flailing segment, the intracardiac sucker is passed well into the left ventricle and enough blood is withdrawn so that the mitral valve is clearly visible. The severed chorda and adjacent margin of the leaflet are grasped with forceps. A 3-0 silk suture is passed through the margin at one end of this untethered segment of leaflet, and the same suture is passed through the margin of the leaflet at the opposite end of this segment (Fig. 1, *b*). The two ends of this suture are then tied down over the redundant intervening leaflet tissue and the ruptured chorda to make a pleat in the redundant segment (Fig. 1, *c*). This segment is thereby shortened, with the result that the remaining intact chordae hold the entire leaflet taut during ventricular systole and eliminate overshooting and incompetence (Fig. 1, *d* and *e*). Several further interrupted sutures are placed to secure the pleat between the free margin of the leaflet and its base. The valve leaflets have been found to be slightly thickened and leathery, and therefore the sutures should hold securely.

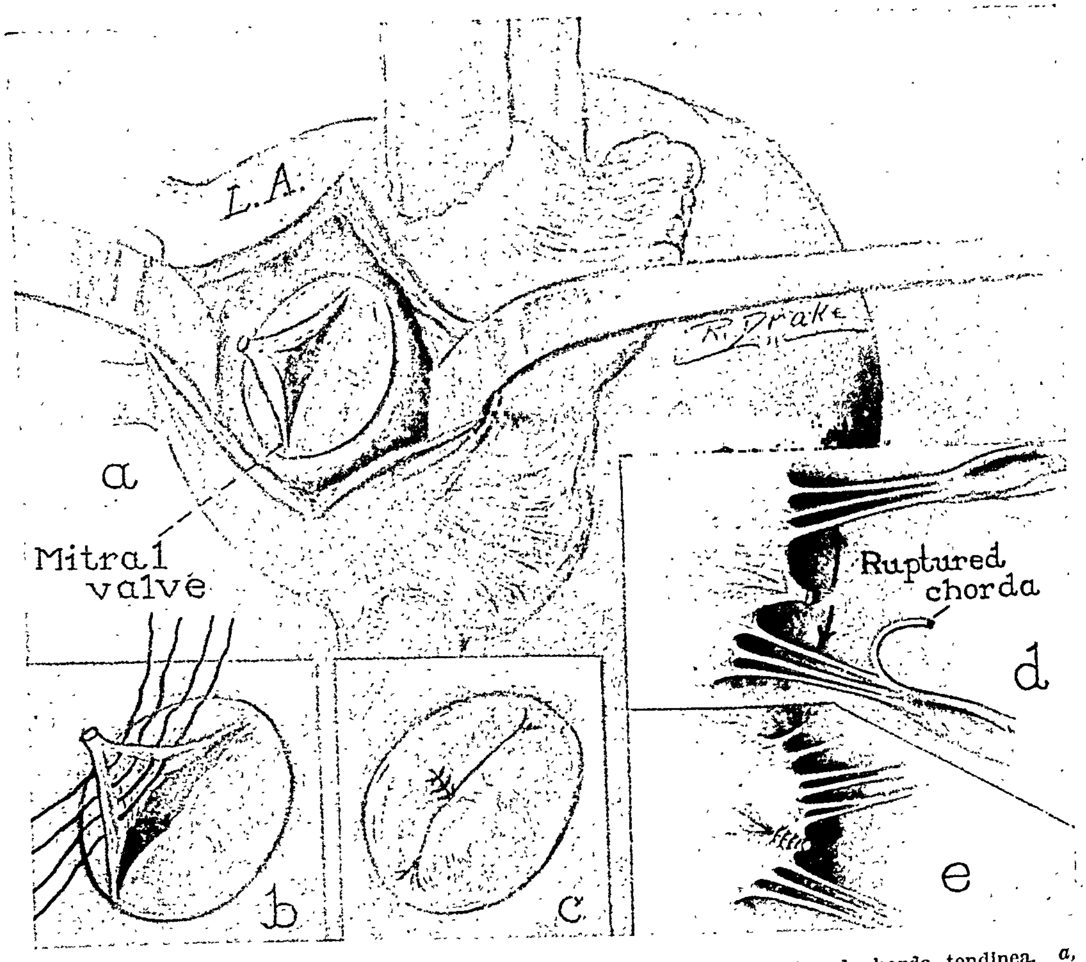

Fig. 1.—Technique of mitral valvuloplasty for repair of a ruptured chorda tendinea. *a*, The exposure of the mitral valve, illustrating a ruptured chorda tendinea. *b*, The placement of sutures to pleat the untethered segment. *c*, Valvuloplasty completed. *d*, Rupture of a chorda tendinea causes a corresponding segment of valve leaflet to be untethered or "flail." *e*, By shortening the flail segment, the remaining intact chordae can prevent eversion of the margin of the entire leaflet during ventricular systole.

When the leaflet has been sutured, the sucker is removed from the left ventricle and the blood level permitted to rise to and above the mitral valve. Then function of the valve is re-evaluated. When satisfactory competence of the valve is established, the left atrium and ventricle are allowed to refill with blood as the atriotomy is being repaired. Thus all air is expelled from the heart. Extracorporeal circulation is then terminated.

CASE REPORTS

CASE 1.—A 53-year-old white laborer had had rheumatic fever as a child and had known of a heart murmur for many years, but significant disability had begun only 6 months before he consulted the Mayo Clinic concerning this difficulty. Sharp, shooting, precordial pain had developed suddenly and was followed by rapid heart action, breathlessness on mild exertion, and orthopnea. He had not worked since that time.

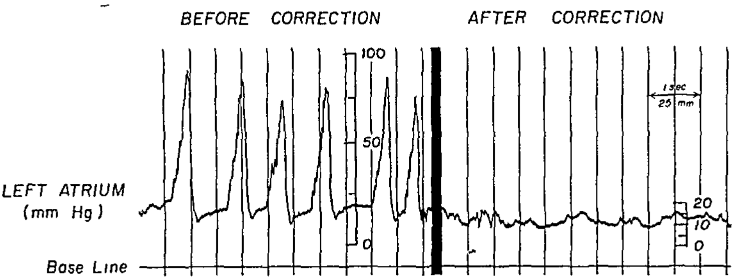

Fig 2.—(Case 1.) Left atrial pressure during operation before and after correction of mitral insufficiency. Only mitral valvuloplasty for the correction of a ruptured chorda tendinea was required to achieve this striking correction of mitral insufficiency.

On examination the classic signs of severe mitral insufficiency were noted. The systolic murmur was well transmitted to the base of the heart, the axilla and the back. There was no evidence of calcification of the valve.

A diagnosis of severe isolated mitral insufficiency was made, probably on the basis of a ruptured chorda tendinea of the posterior mitral leaflet.[9] Open repair of the valve was carried out on Oct 11, 1958, by the technique described. The only valvular abnormality encountered was a ruptured chorda tendinea of the posterior or mural valve leaflet, and this lesion alone required repair. No further procedures were carried out on the valve or valvular ring.

The postoperative recovery was satisfactory, and the patient was dismissed from the hospital on the ninth postoperative day.

A soft, Grade 2, systolic murmur, localized to the cardiac apex and unassociated with a thrill, was noted at each postoperative examination. Since dismissal, the patient has been working steadily and is unaware of any physical limitations except on severe exercise.

The peak pressure in the left atrium was found at operation to be approximately 85 mm Hg before repair, but it fell to approximately 14 mm Hg after repair (Fig 2).

CASE 2.—A 27-year-old farmer had had scarlet fever as a boy, followed by a heart murmur and repeated bouts of rheumatic fever. At age 23, bacterial endocarditis developed, and hemolytic streptococci were cultured from the blood. Later, an embolic occlusion of the right external iliac artery occurred but caused no significant disability. Six months before he registered at the clinic, breathlessness on moderate exertion had developed and paroxysmal nocturnal dyspnea had appeared.

Examination revealed the classic signs of severe mitral insufficiency, and the systolic murmur was well transmitted to the base of the heart and to the back. There was no evidence of valvular calcification. At cardiac catheterization a few days before operation, the pulmonary-artery wedge pressure (Fig. 3) was elevated. This is characteristic of predominant mitral insufficiency. Indicator-dilution curves demonstrated considerable prolongation of the disappearance slope, a finding that also is consistent with a diagnosis of mitral insufficiency (Fig. 3).[10]

A clinical diagnosis was made of mitral insufficiency, due either to a ruptured chorda tendinea or to perforation of a valve leaflet. Repair of the mitral insufficiency was carried out on Jan. 14, 1959.

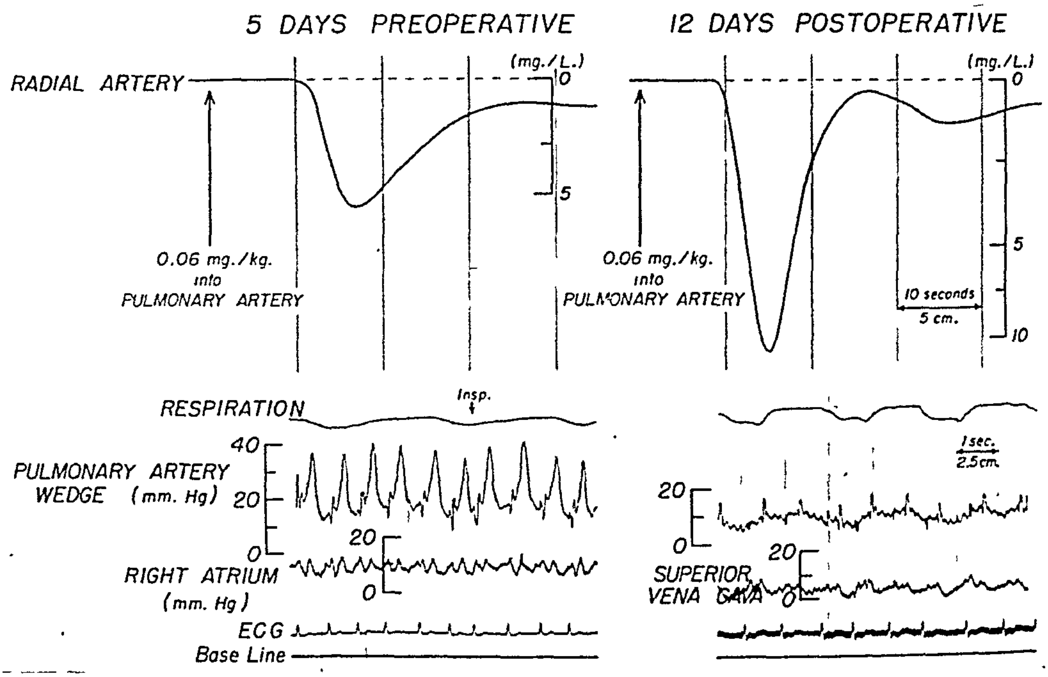

Fig. 3.—(Case 2.) Findings at cardiac catheterization before and after operation. The patient weighed 81 kilograms. Bacterial endocarditis had resulted in rupture of a chorda of the anterior mitral leaflet and a cleft in the posterior leaflet. Repair of the leaflets themselves was all that was required to correct mitral insufficiency.

Operation disclosed that previous bacterial endocarditis had resulted in rupture of a chorda which should normally have been attached to the lateral end of the anterior or aortic leaflet of the mitral valve. A small nodule of calcium on the free margin of the leaflet marked the site of the previous attachment of that chorda. The overshooting of this segment of leaflet was eliminated by the technique described. Exactly opposite this lesion was a wedge-shaped erosion or cleft in the posterior leaflet, and this was repaired by approximating the margins of the cleft with several interrupted sutures of 3-0 silk. When the repair was tested, some distortion of the leaflets was noted which caused gaping and incompetence at the medial commissure. Two sutures were placed in the margins of the adjacent leaflets to achieve partial fusion of this commissure. No further regurgitation through the valve was apparent after this procedure. No sutures were placed in the mitral annulus, and no prosthesis was employed.

Postoperative recovery was uneventful, and the patient was dismissed on the twelfth postoperative day. After operation, a Grade 1 to 2 systolic murmur which was well localized to the apex was present. The heart was quiet, and the patient has remained free of significant cardiac disability.

A peak pressure in the left atrium of 45 to 50 mm Hg was demonstrated at operation before repair, and this was reduced to 16 mm Hg after repair. Postoperative cardiac catheterization on the eleventh postoperative day revealed a pulmonary artery wedge pressure of 11 mm Hg, with a mean pressure of 7 mm Hg. Indicator dilution curves following repair were within normal limits (Fig 3).

COMMENT

Mitral annuloplasty and leaflet substitution by an immobile prosthesis have been employed singly and in combination by those performing open heart surgery for mitral insufficiency.[1-6] This has been true even if one or more ruptured chordae tendineae have been identified as the basic cause of mitral insufficiency. Neither of these procedures seems as anatomically or functionally ideal as does reconstruction of the leaflet proper. The experience reported here demonstrates that, at least in certain instances, repair of the leaflets alone is sufficient to restore valve competence.

It must be stressed, therefore, that the valve leaflets should be carefully observed at the time of operation in the hope that correction of leaflet deformity and function might be accomplished in preference to mitral annuloplasty and replacement of the valve leaflet. When a ruptured chorda tendinea is identified as a cause for mitral insufficiency, the technique described for the repair of this defect should be carried out initially. That mitral insufficiency begets further mitral insufficiency seems clearly established[5] and is due to the fact that progressive dilatation of the mitral annulus may accompany the left ventricular dilatation which results from mitral incompetence. Therefore, although it was not necessary to combine repair of the leaflet with other types of procedures for correction of mitral insufficiency in the 2 cases presented, it seems reasonable to believe that mitral annuloplasty in combination with mitral valvuloplasty may be advantageous in certain instances.

The left atrial pressure tracing before and after valvuloplasty (see Fig 2) strikingly illustrates the fact that function of the valve can be restored by reconstruction of the leaflet alone. The peak pressure of 85 mm Hg in the left atrium recorded in Fig 2 is believed to be the highest left atrial pressure reported and is in sharp contrast to the normal appearance of the tracing after valvuloplasty.

The 2 patients whose cases are reported have not been followed for a sufficient time to permit evaluation of the long term result of mitral valvuloplasty or to answer the question definitively as to whether these sutured leaflets will heal securely. The critical period for possible dehiscence of these repairs probably has passed, however.

SUMMARY

The data presented indicate that mitral insufficiency can be corrected in certain instances by repair of the leaflets of the valve rather than by mitral annuloplasty or replacement of a leaflet with a prosthesis. When mitral insufficiency is due to rupture of one or more chordae tendineae, it may be repaired

by a technique which eliminates the overshooting of the untethered segment of leaflet. This procedure should be carried out as the first step in the correction of this type of mitral insufficiency. The leaflets of the mitral valve must be carefully scrutinized at the time of operation to determine whether or not reconstruction of the leaflet is possible. When it is, this is believed to be preferable to either mitral annuloplasty or replacement of the leaflet by an immobile prosthesis. In certain instances, it is likely that reconstruction of a leaflet and mitral annuloplasty may be beneficially combined.

The 2 patients for whom mitral valvuloplasty alone has been employed for the correction of mitral insufficiency have obtained excellent early results.

ADDENDUM

Recent examination 8 months after operation in Case 1 and a progress report from the other patient indicate maintenance of the initial benefit. In Case 1, the roentgenograms made on the return visit showed striking regression in size of the heart to normal and absence of pulmonary vascular congestion. Both patients continue with full employment.

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THE POSTMORTEM EXTERNAL APPEARANCE OF CONGENITALLY MALFORMED HEARTS AS AN AID TO SURGICAL DIAGNOSIS

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LESS THAN TWO decades ago, the accurate diagnosis of congenital cardiac defects was seldom achieved By utilizing information obtained from electrocardiography, angiocardiography, and cardiac catheterization studies, an exact clinical diagnosis can now often be rendered and a program for surgical correction planned Despite these facilities available for preoperative evaluation of the patient with congenital cardiac disease the surgeon is occasionally confronted at the operating table with an unsuspected anatomic condition of the heart, or one which defies an in situ diagnosis Since this problem usually precludes effective surgical action, we decided to undertake a study of the heart designed to discover whether or not certain external features of the anatomy at autopsy can be related to specific defects

By its very nature, a study based on the postmortem heart imposes certain limitations The external anatomy of the fixed heart is not identical with that of the fresh heart Likewise, the external anatomy of the heart as seen outside the body is not absolutely identical with that inside the body And, of course, the external anatomy of the postmortem heart in situ is not identical with that seen at surgery In spite of these limitations, this work was undertaken and we believe yielded some information useful to the surgeon

MATERIALS AND METHODS

The autopsy material which provided the basis for this study was taken from the Pathology Department at The Children's Memorial Hospital and from the Congenital Heart Disease Research and Training Center of the Hektoen Institute Two hundred and ninety six hearts were selected for evaluation Many additional hearts were reviewed, but because of shapes distorted by fixation and previous study they were not used in this work It must be emphasized that only children's hearts were studied here

The terminology used is adapted from the classification of congenitally malformed hearts previously presented by one of us (M L)[1, 2] Terms used in

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referring to borders, diameters, and certain other external parts of the heart are presented in Fig. 1.

Twenty-two complexes of congenital cardiac disease seen in Table I were studied. Several entities contained in the over-all classification were not considered for this study either because sufficient material was not available, or the condition is one which, at present, is not a diagnostic problem to the cardiac surgeon in the operating room. These are patent ductus arteriosus, vascular rings, adult-type coarctation of the aorta, aortic septal defect, complete transposition with cor biatriatum triloculare, mixed levocardia, dextrocardia, isolated congenital mitral stenosis, and Ebstein's complex.

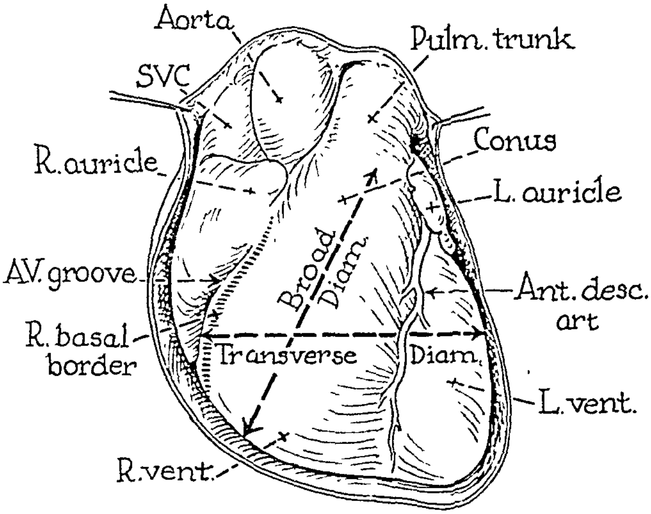

Fig. 1.—Diagrammatic sketch of the normal heart as seen from the anterior view, indicating various landmarks discussed in the text. Note (1) the broad and transverse diameters, (2) the right basal border of the right ventricle, (3) the conus of the right ventricle, and (4) the atrioventricular groove.

Each category of cardiac disease was studied separately. Five external features were chosen as criteria to be evaluated in each heart throughout all of the categories; namely, (1) the over-all shape or outline of the heart as seen anteriorly, (2) the position of the anterior descending coronary artery and its relationship to the formation of the apex of the heart, (3) the size and position of the arterial trunks at the base, (4) the shape of the right basal border of the right ventricle, and (5) the visibility of the left atrial appendage as seen anteriorly. These parts of the external anatomy of the heart are seen in their usual positions in the drawing of the normal heart in situ (Fig. 1).

In a few instances it has been possible to view the exposed heart at the beginning of an autopsy and to evaluate it externally. Such an evaluation has been especially helpful in the study since the distortions of the formalin-fixed specimen are absent.

OBSERVATIONS

The observations made in this study are embodied in the accompanying table. It can be noted that the over-all external features of some complexes aid greatly in their diagnosis, while those of others are less helpful Those in which they aid greatly are tetralogy of Fallot (Fig 2), tricuspid atresia (Fig 3), truncus communis (Fig 4), fetal coarctation (Fig 5), hypoplasia of the aortic tract complex (Fig 5), and total anomalous pulmonary venous drainage (Fig 6)

Tetralogy of Fallot (Fig 2)—In the vast majority of instances in our series, the shape of the heart is either frankly boot shaped, or there is at least a blunting of the apex, giving it a snub nosed appearance The latter is obtained because the apex is formed by both the right and left ventricles, but, mainly, by the right The anterior descending coronary artery forms a shallow S shaped curve The aorta is larger than the pulmonary artery and may or may not appear dextraposed In some, the right basal border of the right ventricle is concave in its upper portion

Tricuspid Atresia Without Transposition With Decreased Pulmonary Flow (Fig 3)—The heart is, in most cases in our series, apple shaped The apex is formed completely by the left ventricle with the anterior descending coronary artery pushed far over to the right The aorta is larger than the pulmonary artery, in most cases the difference in size being very marked The right atrioventricular groove usually is markedly accentuated, and there is a large bulging right atrial appendage

Truncus Arteriosus Communis Persistens (Fig 4)—The hearts in our collection are distinctly egg shaped with a marked increase in the transverse diameter The anterior descending coronary artery originates more in the center of the base rather than on its left side, and as it descends to the apex, it is apparent that both ventricles help form the apex, the left perhaps more than the right There is, of course, a single trunk emanating from the heart with no accessory band on its side

Fetal Coarctation, Hypoplasia of the Aortic Tract Complex, and Total Anomalous Pulmonary Venous Drainage—These hearts can be considered as a group because of their similar external appearance The most important feature here is the marked displacement of the anterior descending coronary artery to the left and posteriorly so that it is barely seen anteriorly, or it is not seen at all (Figs 5 and 6) Thus, the apex is formed exclusively by the right ventricle There is an increase in the broad diameter because the complete anterior aspect of the heart is occupied by the right ventricle The pulmonary artery is larger than the aorta This feature is most marked in hypoplasia of the aortic tract complex (Fig 5) Other external features also serve to distinguish between these complexes In fetal coarctation* and hypoplasia of the aortic tract complex (Fig 5), the anterior descending coronary artery is usually still seen anteriorly This is not true of total anomalous pulmonary venous drainage (Fig 6) The large right atrium and the increase in transverse diameter present in total anomalous pulmonary venous drainage further aid in distinguishing it

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*The complex fetal coarctation is considered here in its pure form This category does not include the transitional form of fetal coarctation in which the left ventricle is of considerable size

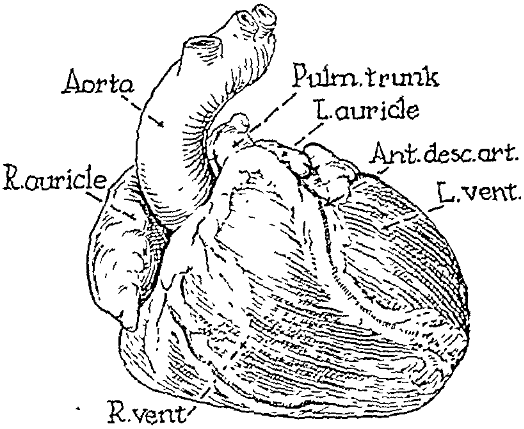


Fig. 2.—Diagrammatic sketch of tetralogy of Fallot as seen from the anterior view. Note (1) apex formed mainly by the right ventricle, (2) S-shaped anterior descending coronary artery, (3) concave right basal border, (4) snub-nosed apex, (5) small pulmonary trunk.

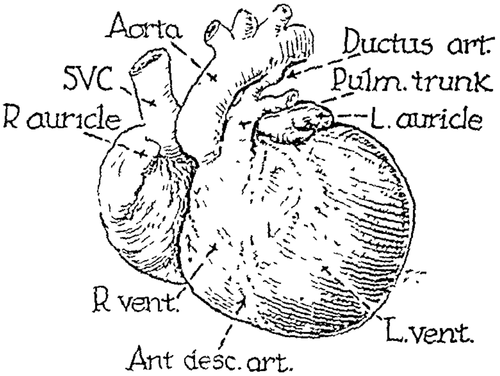


Fig. 3.—Diagrammatic sketch of tricuspid atresia without transposition with decreased pulmonary flow as seen from the anterior view. Note (1) apple-shaped heart, (2) anterior descending coronary artery displaced far to the right, (3) apex formed totally by the left ventricle, (4) deep atrioventricular groove, (5) large, bulging right atrium, (6) small pulmonary trunk.

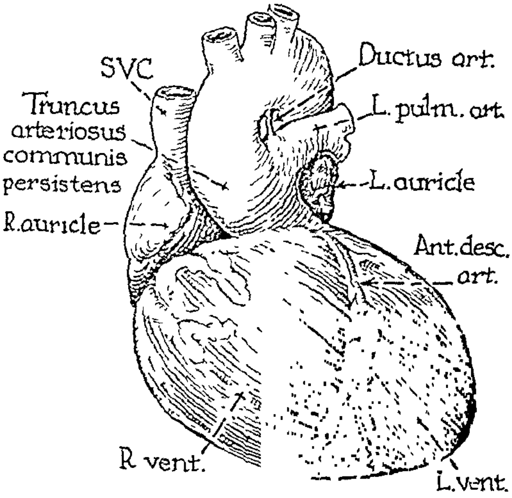


Fig. 4.—Diagrammatic sketch of common truncus as seen from the anterior view. Note (1) egg-shaped heart, (2) single trunk, (3) anterior descending coronary artery commencing more toward the center of the base of the heart.

from the other complexes. In addition, the left atrial appendage is always seen anteriorly in hypoplasia of the aortic tract complex, whereas it is not seen in total anomalous pulmonary venous drainage.

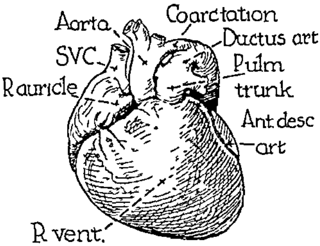
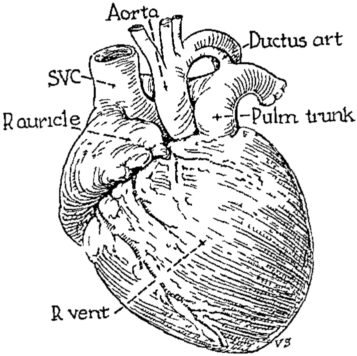


Fig. 5.—Diagrammatic sketch of fetal coarctation as seen from the anterior view Note (1) anterior descending coronary artery displaced far to the left (2) apex formed by the right ventricle, (3) ascending aorta small, but larger than the coarctated area, (4) marked increase in broad diameter.



[illegible] sketch of total anomalous pulmonary venous drainage into the [illegible] vena cava as seen from the anterior view. Note (1) anterior [illegible] it seen anteriorly, (2) very large right ventricle forming the [illegible] both broad and transverse diameters (4) large, bulging right atrium, (5) large superior vena cava (6) pulmonary trunk larger than the aorta

DIFFERENTIATING FEATURES ACCORDING TO ISOLATED CRITERIA

As mentioned above, five criteria were evaluated in this work. Our findings pertinent to these criteria will now be considered.

1. *Anterior Descending Coronary Artery and Formation of the Apex.*—

If one uses this criterion in helping to evaluate the type of congenital heart disease, then the hearts in this series fall into five types: (a) Conditions in which the anterior descending artery is moved considerably to the right with the apex formed by the left ventricle (b) Conditions in which the anterior descending artery is moved slightly to the right or is in normal position with the

TABLE I. TYPES OF PATHOLOGIC COMPLEXES STUDIE

PATHOLOGIC COMPLEX	NO. OF HEARTS STUDIED	LOCATION OF ANTERIOR DESCENDING CORONARY ARTERY	APEX FORMATION	SHAPE OF HEART
1. Tetralogy of Fallot (Fig. 2)	46	Displaced to left, often S-shaped	Mainly by RV and septum with LV contributing to less extent	Roughly triangular or boot-shaped heart; apex snub nosed
2. Partial transposition with pulmonary stenosis or atresia (pseudotruncus) (Fig. 13)	13	Displaced to left, more in atresia than in stenosis	Equally by both ventricles in stenosis; in atresia RV mainly forms apex	Increase in broad diameter
3. Taussig-Bing complex with pulmonary trunk mainly from right ventricle (Fig. 11)	5	In normal position	Totally by LV	Not remarkable
4. Taussig-Bing complex with pulmonary trunk mainly from left ventricle	12	In normal position	Totally by LV in some, and in others, RV contributes but LV predominates	Not remarkable
5. Complete transposition with normal architecture and without ventricular septal defect	24	In normal position or slightly to left	Usually equally by both vents; occasionally RV or LV may predominate	Not remarkable
Complete transposition with normal architecture and with ventricular septal defect (Fig. 8)	15	In normal position or slightly to left	Mainly by LV; occasionally both ventricles contribute equally	Not remarkable
7. Complete transposition with single ventricle and small outlet chamber (Fig. 15)	3	None identifiable	Single ventricle	Not remarkable
8. Complete transposition with ventricular septal defect and pulmonary stenosis	5	Displaced slightly to right	Totally by LV; occasionally RV contributes partially	Not remarkable
9. Truncus arteriosus communis persistens (common truncus) (Fig. 4)	4	Commences more in center of base than on left side	Both ventricles contribute equally or LV slightly more than RV	All hearts egg sha with marked increase in transve diameter
10. Tricuspid atresia without transposition with decreased pulmonary flow (Fig. 3)	20	Displaced far to right on anterior wall	Totally by LV	Apple shaped
11. Tricuspid stenosis with pulmonary stenosis or atresia	12	Displaced far to right on anterior wall	Usually totally by LV; occasionally RV contributes to less extent	Not remarkable

NATOMIC PARTS EVALUATED AND FINDINGS

PULMONARY TRUNK AND AORTA AT BASE OF HEART	RIGHT BASAL BORDER OF RIGHT VENTRICLE	LEFT AURICLE	REMARKS
Aorta larger than PA; normal relative positions, or aorta anterior, and to right	Often concave	May or may not be seen anteriorly	Shape is not an index of pulmonary stenos or atresia
Aorta larger than PA; normal positions, or aorta anteriorly and to right	Not characteristic	Usually seen	
Vessels side by side with aorta right and PA left, or aorta right and anteriorly and PA left and posteriorly; PA larger than aorta	Not characteristic	Usually seen	
As above, or directly anterior-posterior	Not characteristic	Seen in all hearts; displaced right atrial appendage in one case	
Aorta anteriorly and to right; PA posteriorly and to left; PA usually larger than aorta	Not characteristic	Usually seen	
Aorta anteriorly and to right; PA posteriorly and to left; PA usually larger than aorta	Not characteristic	Seen in all hearts	
Aorta anteriorly and slightly to left; PA posteriorly and slightly to right, or vessels anterior-posterior	Not characteristic	May or may not be seen	
PA and aorta in posterior-anterior position; aorta larger than PA	Not characteristic	May or may not be seen	
Single trunk	Not characteristic	Usually seen	
Aorta larger than PA; PA very small; normal relative positions	Not characteristic	Usually seen anteriorly	Right atrioventricular groove usually deepened; right atrial appendage large and *bulging*
Aorta larger than PA; normal relative positions	Not characteristic	Usually seen anteriorly	Atrioventricular groove not deepened; pulmonary trunk may be relatively large as compared to atresia

(Table I continued on next page)

TABLE

PATHOLOGIC COMPLEX	NO. OF HEARTS STUDIED	LOCATION OF ANTERIOR DESCENDING CORONARY ARTERY	APEX FORMATION	SHAPE OF HEART
2. Left coronary artery from the pulmonary trunk	4	Slightly displaced to right	Totally by LV	Not remarkable
3. Isolated atrial septal defect—secundum type (Fig. 12)	12	Displaced to left	Both ventricles contribute equally in young hearts; in older hearts, mainly by RV or totally by RV	Prominent anterior bulge of conus
4. Isolated atrial septal defect—primum type	6	Displaced to left	Both ventricles contribute equally, or mainly by RV	About equal increas in both broad and transverse diameters, bulging conu
5. Isolated ventricular septal defect (Fig. 9)	37	Deviated slightly to right or left depending on dominant ventricle	Usually totally by LV; occasionally equally by both ventricles and infrequently mainly by RV	Conus bulge with increase in broad diameter
6. Hypoplasia of the aortic tract complex	6	Displaced far to left and posteriorly, barely seen anteriorly	Totally by RV	Triangular-shaped heart with marked increase in broad diameter
. Fetal coarctation (Fig. 5)	21	Far to left	Totally by RV	Triangular-shaped heart with marked increase in broad diameter
8. Total anomalous pulmonary venous drainage (Fig. 6)	9	Displaced far to left and posteriorly, not seen anteriorly	Totally by RV	Marked increase in broad and transverse diameters, with conus bulge, anteriorly and superiorly
9. Common atrioventricular orifice (canal) (Fig. 10)	11	Displaced slightly to left, or in normal position	Totally or almost totally by LV	Triangular-shaped heart with increase in both broad and transverse diameters
0. Pure pulmonary stenosis (Fig. 14)	12	Displaced to left and is barely seen	Mainly by RV but LV also contributes; occasionally RV and LV contribute equally	Both broad and transverse diameters increased, but more in transverse
1. Aortic and subaortic stenosis (Fig. 7)	5	Displaced far to right	Totally by LV	Hypertensive shaped heart
2. Idiopathic hypertrophy with fibroelastosis	12	Displaced slightly to right	Usually totally by LV; occasionally RV contributes slightly	Heart roughly pear shaped

(CONT'D)

PULMONARY TRUNK AND AORTA AT BASE OF HEART	RIGHT BASAL BORDER OF RIGHT VENTRICLE	LEFT AURICLE	REMARKS
Normal relative positions	Not characteristic	Not seen	
PA larger than aorta, normal relative positions	Not characteristic	May or may not be seen	
PA larger than aorta; normal relative positions	Not characteristic	May or may not be seen	
PA larger than aorta, normal relative positions	*Rarely concave*	May or may not be seen anteriorly	Apex mainly by RV when defect in pos terior or apical pa of ventricular sept
PA much larger than aorta, *normal relative positions*	Not characteristic	Seen in all hearts	Right ventricle mak up nearly all of th heart
PA larger than aorta, normal relative positions	Not characteristic	Usually seen	Disparity between p monary trunk and aorta; less than i hypoplasia of aort tract complex
PA much larger than aorta	Not characteristic	Not seen	
PA larger than aorta; normal relative positions	Not characteristic	May or may not be seen	
PA about equal to aorta	Not characteristic; 2 cases concave with valvular and infundibular stenosis	Usually seen	
PA larger than aorta	Not characteristic	Usually seen	
PA about equal to aorta in size	Not characteristic	May or may not be seen	

apex formed by the left ventricle. (c) Conditions in which the anterior descending artery is moved slightly or moderately to the left with the apex formed by both ventricles. (d) Conditions in which the anterior descending artery is displaced markedly to the left and posteriorly so that it is barely visible or not seen at all anteriorly. (e) Conditions in which the anterior descending coronary artery is not recognized as such.

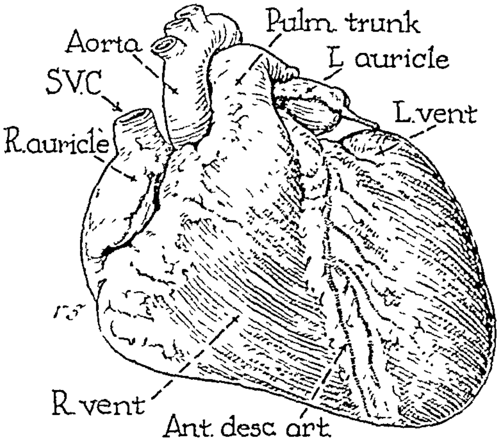


Fig. 7.—Diagrammatic sketch of aortic and subaortic stenosis as seen from the anterior view. Note (1) "hypertensive" shaped heart, (2) anterior descending coronary artery displaced far to the right, (3) large left ventricle forming the apex, (4) aorta smaller than the pulmonary trunk. Refer to Table I for variations.

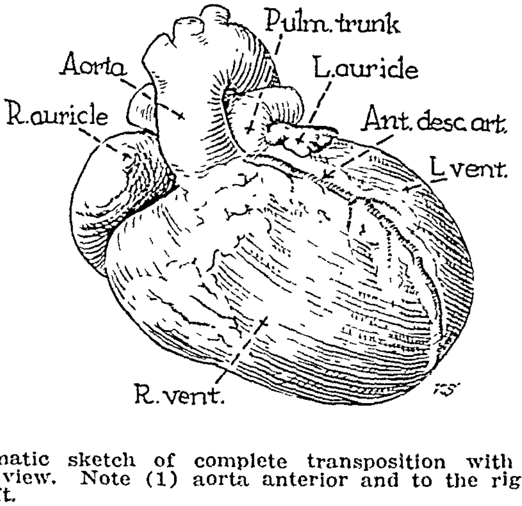


Fig. 8.—Diagrammatic sketch of complete transposition with normal architecture as seen from the anterior view. Note (1) aorta anterior and to the right, and pulmonary trunk posterior and to the left.

(a) Conditions in which the anterior descending artery is moved considerably to the right with the apex formed by the left ventricle. This occurs in tricuspid atresia (Fig. 3) and stenosis complexes, aortic and subaortic stenosis complexes (Fig. 7), and in origin of the left coronary artery from the pulmonary artery. The differentiating characteristics of tricuspid atresia and stenosis complexes are described previously. In aortic and subaortic stenosis, in the small series studied, the pulmonary artery was larger than the aorta. This is not true of aberrant origin of the coronary artery from the pulmonary artery.

(b) Conditions in which the anterior descending artery is moved slightly to the right or is in normal position with the apex formed by the left ventricle. This is seen in complete transposition with normal architecture (Fig. 8), with or without pulmonary stenosis, in the Taussig-Bing complex, and in idiopathic hypertrophy with fibroelastosis. It occurs in some instances of ventricular septal defect (Fig. 9) and common atrioventricular orifice (Fig. 10). Complete transposition and the Taussig-Bing heart (Fig. 11) may be differentiated from idiopathic hypertrophy by the abnormal position of arterial trunks. Ventricular septal defect cannot safely be differentiated from common atrioventricular orifice by external appearance alone.

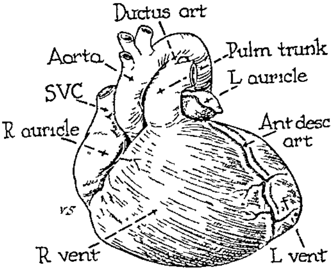


Fig 9.—Diagrammatic sketch of one type of isolated ventricular septal defect as seen from the anterior view. Note (1) large right ventricle, (2) pulmonary trunk larger than the aorta, (3) anterior descending coronary artery displaced a little to the left, (4) apex formed by the left ventricle. Refer to Table I for variations

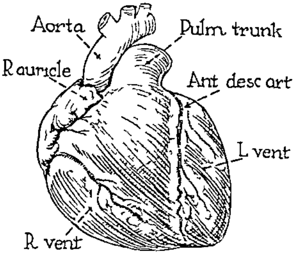


Fig 10.—Diagrammatic sketch of isolated common atrioventricular orifice as seen from the anterior view Note (1) apex formed by the left ventricle, (2) pulmonary trunk larger than the aorta. Refer to Table I for variations

(c) Conditions in which the anterior descending artery is moved slightly or moderately toward the left with the apex constituted by both ventricles This is seen in atrial septal defect (Fig. 12), in some cases of ventricular septal defect and common atrioventricular orifice (Fig. 10), in tetralogy of Fallot (Fig. 2), in partial transposition with pulmonary stenosis (Fig. 13), in some cases of complete transposition with normal architecture (Fig. 8), and in pure pulmonary stenosis (Fig. 14). Tetralogy of Fallot is differentiated as previously stated. Complete transposition is distinguished in this group by the positions of the arterial trunks, and the latter may also serve to differentiate those cases of partial transposition in which the abnormal position of vessels is seen externally. Partial transposition with pulmonary stenosis in which the position of arteries is normal externally may be differentiated from all types of isolated septal defects and pure pulmonary stenosis with large pulmonary artery by the small size of the pulmonary artery in the partial transposition complex. When pure pulmonary stenosis has a small pulmonary artery it may perhaps be differentiated externally from partial transposition with normal position of arteries by the shape and size of the heart. In partial transposition with pulmonary stenosis the heart is in general not enlarged; that is, there is an increase

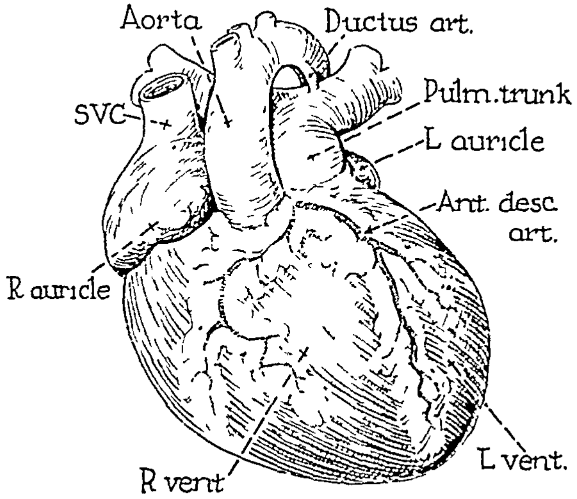


Fig. 11.—Diagrammatic sketch of Taussig-Bing complex as seen from the anterior view. Note (1) apex formed by the left or both ventricles, (2) aorta to the right and slightly anterior, and the pulmonary trunk to the left and slightly posterior, (3) pulmonary trunk considerably larger than the aorta.

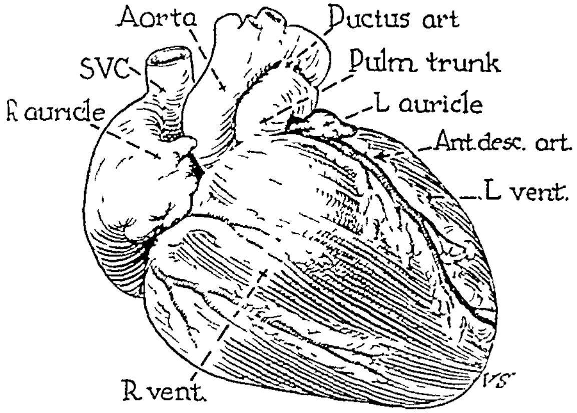


Fig. 12.—Diagrammatic sketch of atrial septal defect of the primum or secundum types as seen from the anterior view. Note (1) large, bulging right atrium, (2) apex formed completely or mainly by the right ventricle, (3) anterior descending coronary artery displaced to the left, (4) anterior bulge of the conus, (5) pulmonary trunk larger than the aorta. Refer to Table I for variations.

in the broad diameter but not in the transverse, while in pure pulmonary stenosis there is an increase in both diameters. It is possible to differentiate atrial septal defect (Fig. 12), ventricular septal defect (Fig. 9) and common atrioventricular orifice (Fig. 10) from pure pulmonary stenosis with large pulmonary artery (Fig. 14) in most cases by the considerable displacement of the anterior descending artery to the left in pure pulmonary stenosis so that it is just seen. It appears to be impossible from this study to differentiate all cases of atrial and ventricular septal defects and common atrioventricular orifice from each other.

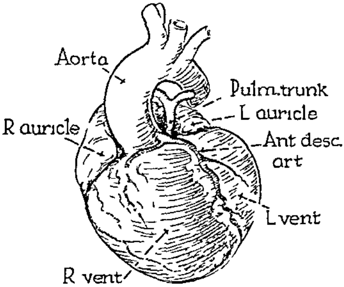


Fig 13 —Diagrammatic sketch of partial transposition with pulmonary stenosis or atresia as seen from the anterior view. Note (1) anterior descending coronary artery displaced to the left with the apex formed mainly or completely by the right ventricle, (2) aorta anterior and to the right Refer to Table I for variations

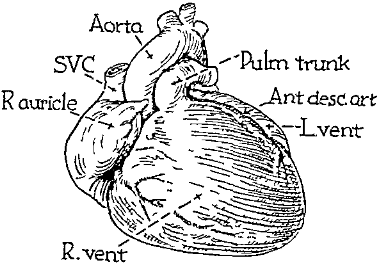


Fig [illegible] as seen from the anterior view No[illegible]ar to the left, but seen anteriorly, ([illegible] trunk about the same size as the aor[illegible]

(d) Conditions in which the anterior descending artery is moved markedly to the left and posteriorly. The complexes included in this category are described above.

(e) Conditions in which the anterior descending artery is not identifiable as such. In the groups studied here only complete transposition with single ventricle and small outlet chamber has this characteristic (Fig. 15).

2. *Size and Position of the Arterial Trunks at the Base.*—

a. *Normal position:* (1) Aorta larger than the pulmonary artery. This is found in some cases of tetralogy of Fallot (Fig. 2), in tricuspid atresia and stenosis (Fig. 3), in some cases of partial transposition with pulmonary stenosis (Fig. 13), and in some instances of pure pulmonary stenosis (Fig. 14). Tricuspid atresia and stenosis and tetralogy have distinct external features previously described. Likewise, pure pulmonary stenosis with small pulmonary artery can be differentiated from partial transposition as described above.

(2) Pulmonary artery larger than aorta. This is seen in hypoplasia of the aortic tract complex (Fig. 5), total anomalous pulmonary venous drainage (Fig. 6), fetal coarctation, atrial septal defect (Fig. 12), ventricular septal defect (Fig. 9), and common atrioventricular canal (Fig. 10). As stated above, the former three can be differentiated, while the latter three cannot always be differentiated from each other.

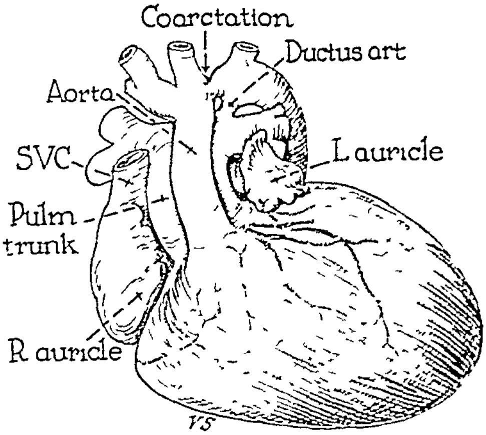


Fig. 15.—Diagrammatic sketch of complete transposition with single ventricle and small outlet chamber as seen from the anterior view. Note (1) the lack of a typical anterior descending coronary artery, (2) aorta and pulmonary trunk in anterior-posterior position. Refer to Table I for variations

b. *Abnormal position of arterial trunks:* The aorta may be (1) slightly dextraposed and hence on the same lateral plane as the pulmonary, (2) the aorta may be anterior and to the right, and the pulmonary artery posterior and to the left, (3) the aorta may be anterior and the pulmonary artery posterior, (4) the aorta may be anterior and to the left, and the pulmonary artery posterior and to the right.

(1) Aorta slightly dextraposed. This is seen in some cases of tetralogy of Fallot and partial transposition (Fig. 13). The former have differentiating characteristics as described above, and were thus differentiated from the latter in this study.

(2) Aorta anterior and to the right, and the pulmonary artery posterior and to the left. This is seen in some cases of the Taussig-Bing heart (Fig. 11) and in complete transposition with normal architecture (Fig. 8). In both of these complexes, the pulmonary artery is larger than the aorta, and the two complexes cannot be differentiated externally.

(3) Aorta and pulmonary artery directly anterior and posterior This is seen in complete transposition with normal architecture with pulmonary stenosis, in some cases of complete transposition with single ventricle and small outlet chamber, and in some cases of the Taussig Bing heart The former is easily differentiated from the latter two by the size of the pulmonary trunk

(4) Aorta to the left and anterior, and pulmonary artery to the right and posterior This is seen only in complete transposition with single ventricle and small outlet chamber in this series

3 *Right Basal Border of the Right Ventricle* —

The concave right basal border of the right ventricle occurs most frequently in tetralogy of Fallot in our series, but also was present in two hearts with ventricular septal defect and in one heart with pure pulmonary valvular and infundibular stenosis

4 *Visibility of the Left Atrial Appendage From the Anterior View* —

In two complexes in this study the left atrial appendage is never seen anteriorly This is in total anomalous pulmonary venous drainage (Fig 6), and in aberrant left coronary artery from the pulmonary artery The left atrial appendage is always seen in this study in hypoplasia of the aortic tract complex (Fig 5) and in complete transposition with normal architecture and ventricular septal defect (Fig 8) In other conditions the left auricle is too variable to be contributory in differential diagnosis

DISCUSSION

From our observations it is clear that the external morphology of the heart is a great aid in diagnosis in tetralogy of Fallot (Fig 2), tricuspid atresia (Fig 3), truncus communis (Fig 4), fetal coarctation (Fig 5), hypoplasia of the aortic tract complex, and total anomalous pulmonary venous drainage (Fig 6) It is also evident that the position and size of the arterial trunks, and the course of the anterior descending coronary artery may be an aid to the diagnosis of a complex

From the surgical point of view, it may be necessary to differentiate tetralogy of Fallot, partial transposition with pulmonary stenosis or atresia, truncus communis, and pure pulmonary stenosis It may be possible to differentiate tetralogy of Fallot (Fig 2) from partial transposition with pulmonary stenosis (Fig 13) (double outlet right ventricle) in children In tetralogy of Fallot, the concave proximal border of the right ventricle and the snub nosed apex are characteristically present, while these are characteristically absent in the latter The number of partial transpositions studied in this series, however, is too small to reach a more definite conclusion Likewise, it may be possible to differentiate truncus communis from pseudotruncus In this series, true truncus had a characteristic egg shaped heart with the anterior descending artery starting in the middle of the base of the heart (Fig 4) Pseudotruncus (partial transposition with pulmonary atresia) (Fig 13) was not characterized in this way were excised for histologic analysis. Examination of the in situ specimen revealed no apparent abnormality of the cardiopulmonary system, and all lines of anastomosis were smooth and well healed. On opening the heart, an old, organized, occluding thrombus was found in the superior pulmonary vein; this was probably an early postoperative event. There had been no clinical or radiographic evidence of massive venous congestion or infarction at any time in the postoperative period. The normal appearance of the operated lung at postmortem also ruled out these changes.

Fig. 2.—Angiocardiogram made 35 months after autotransplantation showing normal pulmonary circulation bilaterally

Histologic Examination.—

Numerous comparable longitudinal and cross sections were taken from the main bronchi, pulmonary arteries and veins, and from more peripheral areas of both lungs. These were subjected to various histologic staining techniques and mounted for microscopic analysis. Silver impregnation was used on some sections to show the nerve tissue elements of the lung and pulmonary vessels.

The following observations were made.

Right main bronchus: The nerve fibers proximal and distal to the suture were not numerous. There was evidence of regeneration across the suture line.

Distal to the suture, numerous partially regenerated distal stump fascicles were seen. The axons were predominantly of small caliber, 1 to 2 μ; but some were of larger caliber, 4 to 5 μ The latter were thought to be pre-ganglionic fibers No ganglion cells were seen

Right upper bronchus (Fig. 3): Numerous well-impregnated nerve bundles are present external to cartilage and are usually seen coursing along side arteries Some fascicles appear to be incompletely filled with nerve fibers A section through a portion of the middle lobe showed essentially the same pattern.

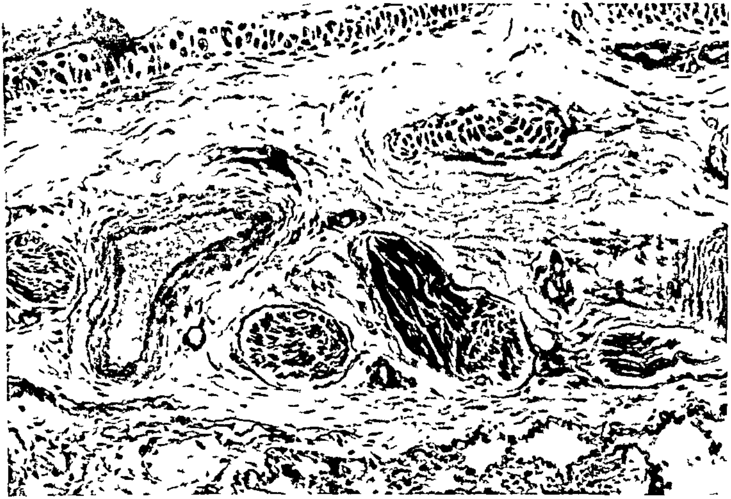


Fig 3 —Photomicrograph of a section of the right main bronchus distal to the suture line Note presence of peri-arterial nerve bundles with incomplete filling of some fascicles (×200, reduced ¼)

Right pulmonary artery: Nerve fibers could be seen crossing in the connective tissue across the suture line Fibers were more numerous proximal to the suture line

Comparative sections of pulmonary parenchyma of both sides showed no essential difference between the right and left lung

DISCUSSION

Section of the main bronchus would transect pre-ganglionic vagal, afferent vagal, and post-ganglionic sympathetic fibers It was concluded from analysis of slides that regeneration across the suture line had occurred What percentage and what kind of fiber successfully regenerated is impossible to determine in this type of study. It was clear, however, that there were nearly as many fibers coursing along the secondary and small bronchi on the side operated upon, as there were in the case of the normal left side. The absence of the Hering-Breuer reflex, however, indicates an absence of *functional* regeneration of afferent nerve fibers.

Functionally and anatomically, the denervated lung appeared not significantly different from the normal one after this time lapse. The moderate deficiency in oxygen uptake is consistent with the relative ventilation in this lung and is probably due to postoperative parietal restriction.

Examination of the serial radiographs from angiocardiography indicated no gross difference in rate or volume of blood flow in the denervated lung insofar as this interpretation can be made from dye distribution. In addition, the oxygen uptake paralleling the ventilation would suggest a normal pulmonary artery flow on this side.

SUMMARY

1. Anatomic and physiologic observations are reported in a dog which was sacrificed 35 months after successful autologous replantation of an excised lung.
2. Bronchospirometric studies revealed only moderate loss of pulmonary function in the replanted lung.
3. A loss of the Hering-Breuer reflex of the replanted lung was demonstrated and this was taken as representing failure of afferent vagal regeneration.
4. Examination of the cardiopulmonary system of the sacrificed dog revealed no gross abnormality, other than a thrombosed superior pulmonary vein on the side operated upon.
5. Microscopic study of the replanted lung showed regeneration of nerve elements across the suture line. The physioanatomic classification of the regenerated element could not be determined in this study. The histologic findings of the lung operated upon were otherwise normal.

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THE MANAGEMENT OF BRONCHOPLEURAL FISTULAS

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BRONCHOPLEURAL fistula is the most dreaded complication of pulmonary surgery Although uncommon in nontuberculous pulmonary surgery, the incidence of bronchopleural fistula in resection for pulmonary tuberculosis varies widely in the current literature The average incidence, from collected papers between 1951 and 1958, is 6 8 per cent[1] In our own hands in 200 consecutive resections for pulmonary tuberculosis, 2 cases were complicated by fistula and 1 of these patients died in spite of active surgical management Once a bronchopleural fistula occurs, a mortality rate of around 30 per cent[2] is common, irrespective of how it is managed This complication is the commonest cause of postoperative morbidity and mortality and constitutes the greatest hazard in resection for pulmonary tuberculosis

Because of the controversy in the literature about the management of bronchopleural fistulas, we felt that our experience in the management of 10 patients, 8 of whom were originally operated upon by other surgeons, is worthy of analysis No attempt will be made to emphasize the etiology and diagnostic features nor the pathogenesis[3] since these have been well documented

CASE REPORTS

CASE 1 —F S , a 36 year old woman had had a right upper lobectomy for fibrocaseous disease in 1952, which was complicated by incomplete re expansion She was discharged with a large apical space and was re admitted 2 years later with positive sputum, drug resistant organisms, and a persistent right apical space Bronchography revealed a large right upper lobe stump communicating with the apical space (Fig 1)

The right chest was re opened and a large empyema pocket was mobilized extrapleurally The long residual stump was amputated, flush with the main bronchus, and closed with No 36 wire on an atraumatic Sellors needle The apical segment of the lower lobe, which was grossly involved in fibronodular disease, was resected Both the stumps were carefully covered with viable peribronchial tissues The procedure was completed with a five rib osteoplastic thoracoplasty to obliterate the dead space Recovery was uneventful sputum became negative, and the patient was subsequently discharged well

Comment —In the presence of a long stump and a large apical space, conservative management over a 2 year period was not effective and, indeed,

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should not have been persisted with. Re-amputation of the bronchus stump, combined with a space-reducing procedure, was the only alternative.

Case 2.—S. C., a 42-year-old man, had been treated since late 1930 for cavitary disease in the right upper lobe and apical segment of lower lobe. Eight-rib thoracoplasty in stages

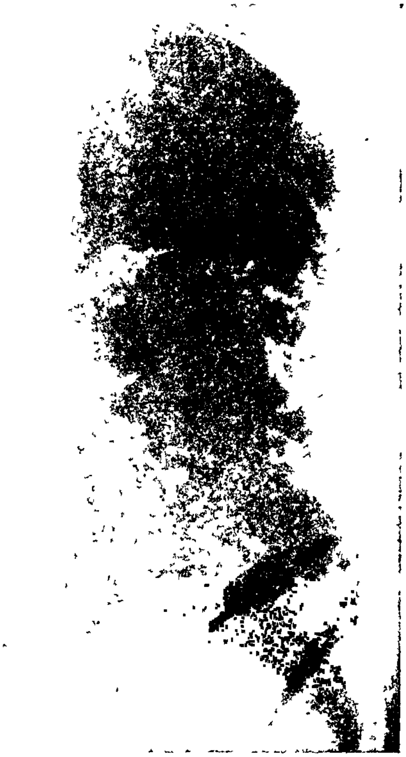


Fig. 1.—(Case 1, F. S.) Bronchogenic demonstration of the long residual stump of the right upper lobe bronchus.

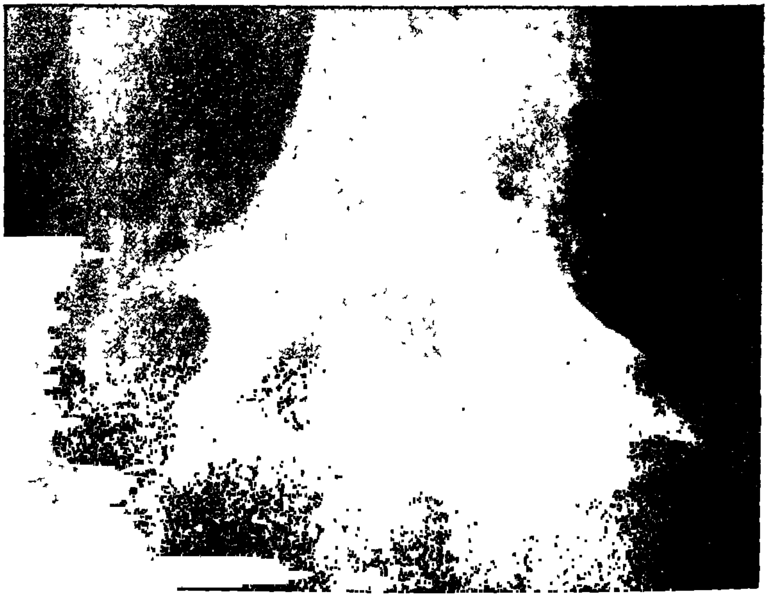


Fig. 2.—(Case 2, S. C.) Sinogram which demonstrates the long residual right main-stem bronchus.

failed to convert sputum. In 1953, he was still sputum positive and now drug resistant. A right pneumonectomy was performed. Resection was complicated by bronchopleural fistula. Conservative management, including tube drainage, broad spectrum antibiotics, and all available antituberculous drugs, failed to heal the fistula. During the next 4 years the sputum remained positive and there were several episodes of contralateral spread.

This patient came under our care in 1957 with a bronchopleurocutaneous fistula, a positive sputum, and resistance to all drugs. Bronchoscopy and sinogram showed a long bronchus stump. At the time of pneumonectomy, the upper and lower lobe bronchi had been closed separately, thus leaving a stump at least 4 cm. in length (Fig. 2).

The right chest was reopened through a posterolateral incision. Several hours were spent in mobilizing the fistulous tract. No anatomic landmarks could be identified and the hilum was a mass of fibrous tissue. At the end of 3 hours, the procedure was abandoned. This patient continues to have a draining sinus and is intermittently positive.

A B

Fig. 3.—(Case 3, L. B.) A, A view of the chest made 5 weeks after conservative management of the bronchopleural fistula. B, Posteroanterior view of the chest after a tailoring thoracoplasty.

Comment.—The indication for surgical intervention in this case is clear cut. Technically, however, it was felt to be too hazardous to continue at that time. With increasing experience, this patient could have been approached more favorably through an anterior thoracotomy or a median sternotomy incision. By this approach, the hilar vessels can be ligated inside the pericardium and the right main bronchus and its fistula can be safely approached through more normal tissue planes.

Case 3.—L. B., a 25 year old man was admitted with an open cavitary lesion in the left apex. After 4 months of drug therapy, the left apicoposterior segment was resected by us. Resection was complicated by a staphylococcal empyema and a bronchopleural fistula. Intercostal tube drainage and massive doses of broad spectrum antibiotics were immediately instituted. Six weeks later, a standard five rib thoracoplasty was performed. Following this, the fistula healed. The patient was subsequently discharged cured.

Comment.—In this case, 6 weeks of conservative treatment with tube drainage and antibiotics failed to heal the fistula. More active surgical measures were necessary.

CASE 4.—J. W., a 46-year-old man, had been in the sanatorium for over 10 years and at one time had far-advanced disease involving both lungs. The disease in the left lung had been arrested following a seven-rib thoracoplasty. The presenting problem was a destroyed right upper lobe and apical segment of the lower lobe with cavitation. Sputum was positive and drug resistant. Ventilation studies showed a total vital capacity of 45 per cent and maximum breathing capacity of 16 per cent of predicted values. The right upper lobe and apical segment of the lower lobe were resected and a five-rib tailoring thoracoplasty performed by us. During the early postoperative period, the right upper lobe bronchus broke down. Tube drainage and broad spectrum antibiotics were immediately started. Tracheotomy was done to combat ventilatory insufficiency and prevent contralateral spillage. After 6 weeks, there was no improvement, so the stump, which had been originally closed with silk, was re-exposed, sutured with wire, covered with a viable muscle graft and a Schede thoracoplasty was performed. Two weeks later death occurred from sudden uncontrollable hemorrhage inside the right chest.

Comment.—Permission for autopsy in this case could not be obtained. The cause of the hemorrhage is not definitely known, but very likely this was secondary hemorrhage from the pulmonary artery in an infected space.

CASE 5.—E. T., a 38-year-old woman, had been in the sanatorium for over 9 years and had been through five thoracotomies involving both sides. In 1956, she had presented with a positive sputum and drug resistant organisms. A bronchogram showed a bronchopleural fistula from the left apicoposterior stump communicating with an empyema pocket extending up under the thoracoplasty (Fig. 4). The left chest was re-opened and the remainder of the left upper lobe, together with the empyema pocket, was mobilized extrapleurally. The left upper lobe bronchus was divided flush with the main bronchus. The bronchus stump was closed with wire and then covered by a muscle graft. The existing apical thoracoplasty was revised and extended. She made an uneventful recovery and was later discharged.

Comment.—Eighteen months after discharge she returned with *one* positive sputum. Further investigations failed to show either reactivation or recurrence of fistula.

CASE 6.—L. W., an 18-year-old girl, was admitted in 1950 with a tuberculoma in the apical segment of the left lower lobe and was treated by segmental resection. Resection was complicated by massive atelectasis, empyema, and bronchopleural fistula. Four years later, a left pneumonectomy was performed because of persistent fistula. Infection of the left pleural space persisted and the bronchus stump broke down. Seven-rib thoracoplasty in stages was followed with an immediate good result. One year later she developed a draining sinus and sputum became positive again. Bronchoscopy and bronchography showed a long left main-stem bronchus stump communicating with the skin. Through a left anterior thoracotomy, the hilum was explored. The left pulmonary artery was ligated inside the pericardium, then the bronchus stump was isolated and dissected up to the carina. The fistulous stump was amputated flush with the trachea and closed with wire. This girl made an uneventful recovery.

Comment.—A standard posterolateral approach in this case would have presented technical problems similar to those encountered in Case 2.

CASE 7.—J. T., a 28-year-old man, underwent right upper lobectomy for a cavitary lesion. Resection was complicated by empyema and bronchopleural fistula. A tailoring thoracoplasty 4 weeks later failed to heal the fistula. About 18 months later, the fistula was explored and the bronchus stump was re-amputated and the thoracoplasty revised and extended. The fistula recurred. In spite of tube drainage and antibiotics, the patient continued to go downhill and had repeated contralateral spreads. At this stage, the patient came under our care. We recommended right pneumonectomy, which was not acceptable to the patient who soon afterward left the sanatorium against advice.

CASE 8.—L. C., a 35-year-old man, with severe diabetes, was admitted in September, 1951, with cavitary disease in the left upper lobe and was treated with a left upper lobectomy after 6 months of chemotherapy. Recovery was uneventful. He was re-admitted in 1955 with cavitation in the apical segment of the left lower lobe. Following a course of antituberculous drugs, a left pneumonectomy was performed in November, 1956. This was complicated by bronchopleurocutaneous fistula. Eight-rib thoracoplasty in stages and a stage of Schede thoracoplasty failed to heal the fistula. Two episodes of contralateral spread occurred. In late 1958, this patient was presented to us with positive sputum, positive draining sinus, and drug resistant organisms. A long left bronchus stump, communicating through an empyema pocket to the skin on the chest wall, was demonstrated (Fig. 5).

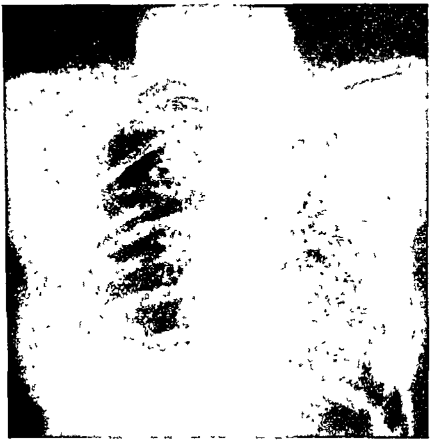
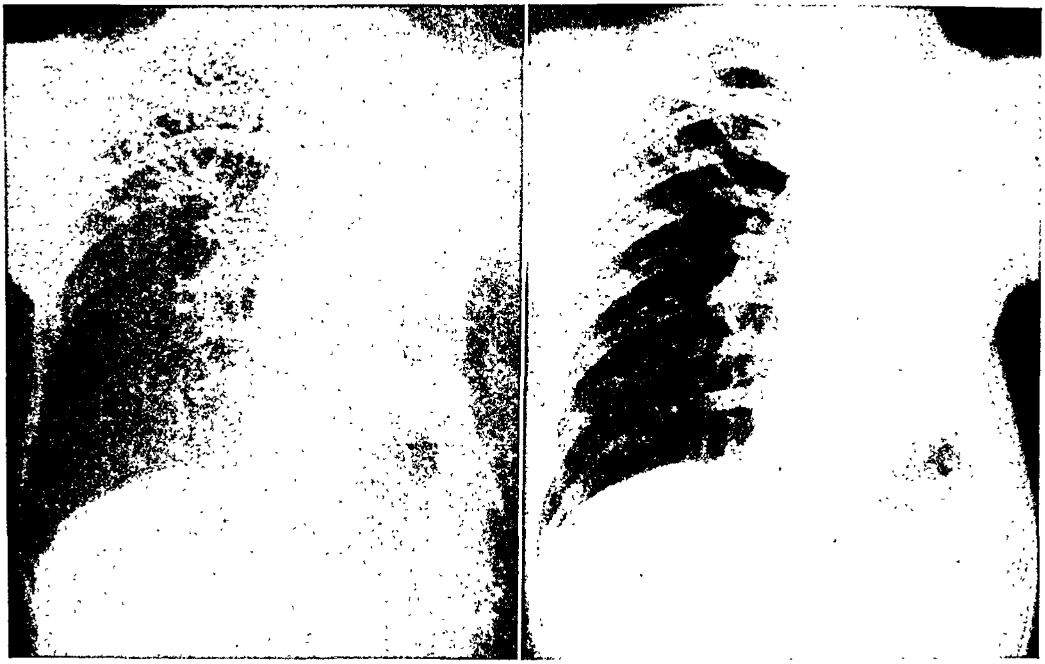


Fig 4.—(Case 5, E T.) Bronchographic demonstration of the fistula extending up under the thoracoplasty.

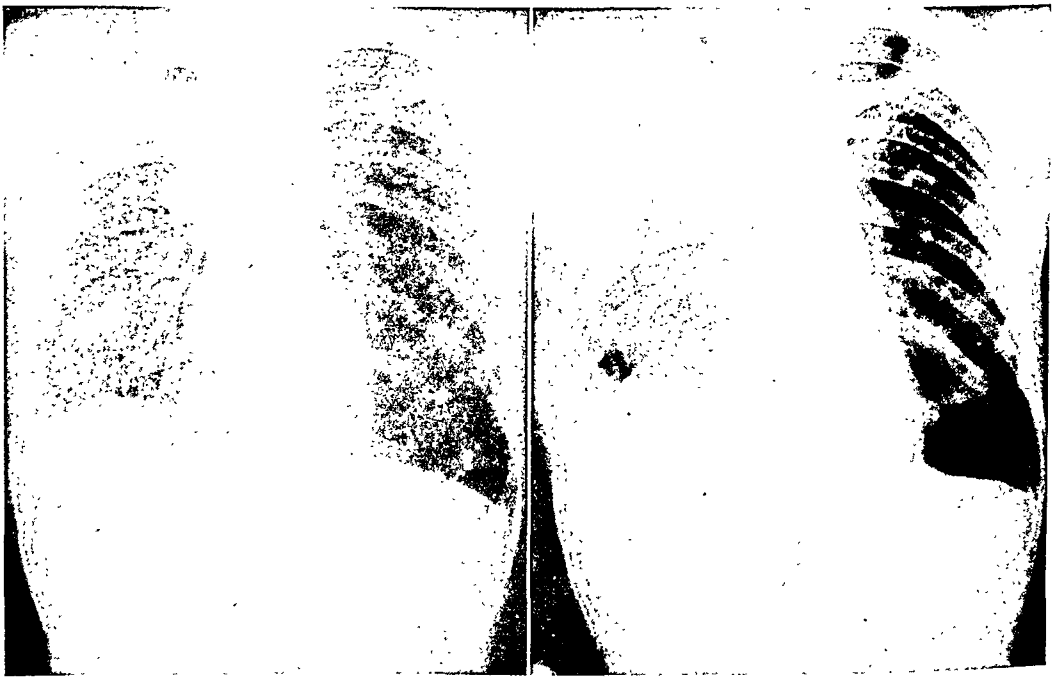
Re-amputation of the fistulous stump was carried out through a left anterior L-shaped incision dividing 3, 4, and 5 costal cartilages. The pericardium was deliberately opened and the left hilar vessels ligated inside the pericardium. The left main-stem bronchus was mobilized up to the carina and transected flush with the trachea. The bronchus stump was closed with wire and adequately covered with viable tissue. This patient made an uneventful recovery and is ready for discharge.

Comment.—In this case it was clearly demonstrated that it would have been difficult if not impossible to revise the bronchus stump through a classical posterolateral approach. Again it would have been extremely dangerous to dissect the bronchus without prior ligation of the pulmonary artery and veins, since all these structures were densely bound by fibrous scar tissue to the region of the bronchus stump.



A. B.

Fig. 5.—(Case 8, L. C.) *A*, Roentgenogram of the chest, following a sinogram, which demonstrates a long left bronchus stump and a normal right bronchial tree. *B*, Postoperative x-ray study after the fistula has closed.



A. B.

Fig. 6.—(Case 9, S. G.) *A*, Bronchographic demonstration of the fistula in the right upper lobe bronchus stump communicating with the apical space. *B*, Postoperative roentgenogram.

CASE 9—S G, a 29 year old man, was treated for bilateral apical disease from 1950 to 1954, and re admitted in 1956 with reactivation of disease After 14 months of treatment with drugs, a right upper lobectomy was carried out A residual space persisted and the sputum became positive Bronchography revealed a bronchopleural fistula (Fig 6)

The right chest was re opened and the empyema sac was mobilized extrapleurally The bronchus stump was re amputated, flush with the main bronchus, and closed with wire After covering the stump, a five rib osteoplastic thoracoplasty was performed There was an uncomplicated recovery

Comment—The right upper lobe bronchus stump breaks down more frequently as is noted in Cases 1, 4, and 7, but, as the right upper lobe is the commonest lobe to be resected for pulmonary tuberculosis, this susceptibility may be more apparent than real

CASE 10—R M, a 54 year old man, was treated with drugs for 2 years for a right apicoposterior lesion The lesion was removed by a large wedge resection Following resection, sputum became positive and a small apical pocket persisted Bronchography revealed a bronchopleural fistula communicating with the apical pocket

The right chest was re opened and the remainder of the upper lobe along with the apical empyema was mobilized extrapleurally The upper lobe bronchus was divided flush with the main bronchus and closed with wire After covering the stump with a large pedicled pleural flap, a tailoring thoracoplasty was done The postoperative course was complicated by severe paradoxical breathing recurrent atelectasis, and ventilatory insufficiency but these responded to tracheostomy and chest strapping

Comment—In this elderly man, a standard tailoring thoracoplasty was performed instead of the osteoplastic type which we prefer, because the latter procedure is more time consuming and the patient's condition on the table was deteriorating A tracheostomy 2 days later was a life saving procedure

DISCUSSION

The management of bronchopleural fistula is still a controversial subject Pacheco and his associates[4] recommend conservative management while others[5] favor immediate re operation Conservative management is probably worth a trial initially When a fistula is recognized, simple intercostal tube drainage should be immediately instituted to minimize spillage into the remainder of the lung or the contralateral lung The problem of spillage assumes grave significance when fistula occurs in a pneumonectomy stump As a prophylaxis, in all pneumonectomies, it has been our practice to keep the pleural space dry for 2 to 3 weeks When a partial resection is complicated by fistula intercostal tube drainage and negative suction is instituted immediately in an attempt to re expand the remainder of the lung and obliterate the pleural space Broad spectrum antibiotics are used liberally to combat the almost inevitable superimposed pyogenic infection

Tube drainage and antibiotics constitute the early conservative therapy A small leak occurring in a segmental stump is very likely to heal with this regimen A fistula in a major bronchus may close only temporarily, leaving a residual pleural space It is probably acceptable to continue conservative management of such a space in the nontuberculous patient In a tuberculous patient, however, the fistula may remain masked temporarily but, in time, the majority of these patients will return with a positive sputum, drug resistant organisms, and possibly spread to other areas. Once a major fistula becomes established, definitive surgical methods should be resorted to after 4 to 6 weeks. Each patient with a bronchopleural fistula presents a different problem and, as such, no generalization in their surgical management can be made.

Established bronchopleural fistulas can be broadly separated into three groups:

(1) *Fistula occurring after segmental resection:* This is usually seen after apical or apicoposterior segmental resection. If recognized early and treated with tube drainage and suction, the majority of these will close if superimposed infection can be controlled. If the fistula does not heal in 4 to 6 weeks, a standard or osteoplastic thoracoplasty will close the fistula. Rarely, if the fistula has been long standing and associated with a thick empyema sac, will thoracoplasty alone be inadequate but must be combined with decortication of the sac.

(2) *Fistula occurring in a major bronchus following lobectomy:* For some reason the right upper lobe stump seems to be more vulnerable to breakdown. In spite of initial treatment with drainage, suction, and antibiotics, the fistula is more likely to persist and more active surgical measures will be necessary. Complete excision of the infected space, re-amputation of the fistulous stump, if long, and a space-reducing procedure are all necessary for a satisfactory result.

(3) *Fistula in a pneumonectomy stump:* Three of the above cases were in pneumonectomy stumps. These patients had a very long term, indeed too long a trial, of conservative treatment. Drug resistant organisms, positive sputum, a draining sinus, low-grade sepsis, and repeated contralateral spread are the dominant features in them. Re-amputation of the bronchus stump, closure with wire, adequate coverage of the bronchus, and obliteration of the pleural space will close the fistula in most instances.

In all 3 patients with fistulas following pneumonectomy, multiple stages of thoracoplasty had been performed several years before. These cases present considerable technical difficulty. Long-standing sepsis makes it virtually impossible to isolate the vascular structures in the distorted hilum, and, because of this, the bronchus stump cannot be dissected with safety. Under such circumstances it is our practice now to approach the hilum through a median sterniotomy or an anterior thoracotomy and to re-ligate the pulmonary artery and veins inside the pericardium as the first step. After this, the bronchus stump can be dissected up to the carina with impunity and the repair completed with relatively little risk. It is felt that an anterior approach such as this, with control of the major vessels from within the pericardial sac, will allow more of these complicated fistulas to be successfully eliminated.

In the final analysis, the management of bronchopleural fistulas is preventive. More careful attention to the bronchus stump initially will reduce the number of breakdowns to an irreducible minimum Thus, it behooves one to reiterate the principles of bronchus closure These are—as short a bronchus stump as possible, a viable stump, as little suture material as possible, preferably of wire, and careful coverage of the bronchus with a viable pleural, pericardial or muscle flap[1] These measures, combined with the principles of surgical technique as usually practiced, will improve the still too high incidence of bronchopleural fistula

SUMMARY

The management of 10 cases of bronchopleural fistula is discussed Eight of these were long standing cases

Four occurred following right upper lobectomy, 3 following pneumonectomy, 2 following resection of the left apicoposterior segments, and 1 after a large wedge resection of the right apex

One patient (Case 4) died, 1 (Case 7) refused further surgery, in 1 (Case 2) the fistula could not be closed The remaining 7 healed following active surgical measures

If the fistula persists after 4 to 6 weeks of conservative treatment with tube drainage and antibiotics, more definitive surgical procedures should be adopted forthwith The principles of bronchus closure are re stated as the real management of bronchopleural fistula is preventive

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MEDIASTINAL TERATOMA IN INFANCY

Report of Successful Removal From Premature Infant and Review of Literature

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THE DEVELOPMENTS in thoracic surgery during the past two decades and the more frequent use of periodic chest x-ray examinations have stimulated renewed interest in teratomas of the mediastinum. The literature on the subject largely concerns adults, with a relatively small number of cases reported in childhood. In infancy, the tumor is a comparative rarity, and only a few tumors have been successfully removed during this early period of life. Today, it should be possible to remove safely most large symptomatic mediastinal teratomas in infants if the condition is suspected and surgery is undertaken without unnecessary procrastination.

After the gonads, the mediastinum is the most common site for teratomas n man. These tumors have been the center of great interest in the past beause of their extraordinary morphology. Their true incidence in relation o other primary tumors of the mediastinum varies among different reported eries. In general, however, they rank second after neurogenic tumors, alhough, in some reviews, tumors of the thymus occupy this position. Granulomas and lymphomas are not considered in this review of primary mediastinal tumors.

The comparative incidence of primary mediastinal tumors differs in some areas between the infant and the adult. Teratoma appears to be the most common tumor occurring in the anterior mediastinum of infants and children. Although the thymus casts a prominent mediastinal shadow during the first year or two of life, true thymomas are uncommon in infants. Two other relatively common anterior mediastinal tumors found in adults—substernal thyroids and pericardial cysts—are rarely encountered in infants.

Recent experience with a large mediastinal teratoma which was successfully removed from a 2-day-old premature infant stimulated our interest in this subject. From a review of all available literature, this appears to be the youngest individual from whom such a tumor has been successfully removed. After a short period of temporary improvement, the infant developed progressively severe respiratory distress due to a paralyzed left diaphragm. This

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desperate situation was corrected surgically by infolding the diaphragm, using a reinforcing prosthesis of knitted Dacron mesh Because of the rarity of this tumor in the newborn and certain interesting features encountered in this patient, it was felt worth while to record this experience and to review the pertinent literature

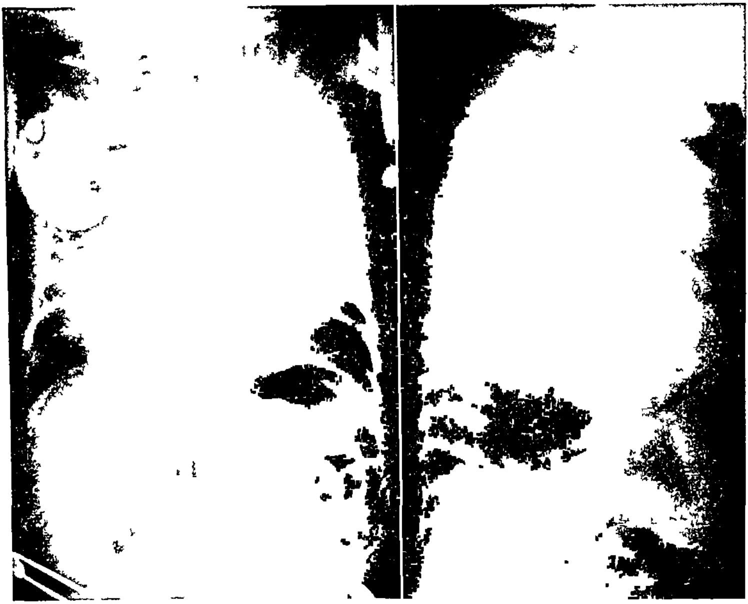

Fig 1—Chest roentgenograms made Nov 24 1958 Posteroanterior and lateral views which show large mediastinal teratoma

CASE REPORT

J F, a white female was born prematurely in the Buffalo Children's Hospital on Nov 22 1958, in the seventh month of pregnancy following spontaneous rupture of the membranes The pregnancy otherwise had been uneventful Birth weight was 5 pounds, 7 ounces The obstetrician commented upon the excess mucous and costal retraction In the premature nursery the infant's color was dusky when temporarily removed from the Isolette During the first day, moderate respiratory distress continued with xyphoid retraction and transient episodes of cyanosis Breath sounds were noted to be diminished over the left chest No cardiac bruits were heard The possibilities of atelectasis or hyaline membrane disease were entertained On the second day, the left hemithorax was noted to be dull to percussion with absent breath sounds Chest x ray studies obtained that afternoon Nov 24, 1958, showed a large homogeneous mass with a sharp lower border The mass occupied most of the left hemithorax displacing the mediastinum to the right (Fig 1) The infant was taken to the operating room that evening with a preoperative diagnosis of mediastinal cyst or tumor. A nasogastric tube passed easily into stomach, but no special diagnostic studies were performed because of the precarious condition of the infant.

The chest was opened through the complete length of the fifth interspace. A well-encapsulated dark, red, solid mass, which practically filled the entire left hemithorax, presented. It was necessary to divide the fifth rib to expose adequately the base of this mass. A number of large vessels entering the tumor from the mediastinum were divided. A one centimeter adherent piece of pericardium was removed with the tumor. A relatively normal-sized thymus remained undisturbed in the anterior mediastinum. The entire left lung, which had been compressed inferiorly, now expanded well with massage and gentle positive pressure. For no apparent reason, the heart remained largely in the right hemithorax after the tumor was removed. The vessels that had coursed to the tumor appeared to originate from the mid anterior and superior areas of the mediastinum. Because of the infant's unstable condition the mediastinum was not examined further. The immediate postoperative chest roentgenogram showed the left lung to be well expanded and the left diaphragm not elevated. The heart remained largely shifted to the right (Fig. 2).

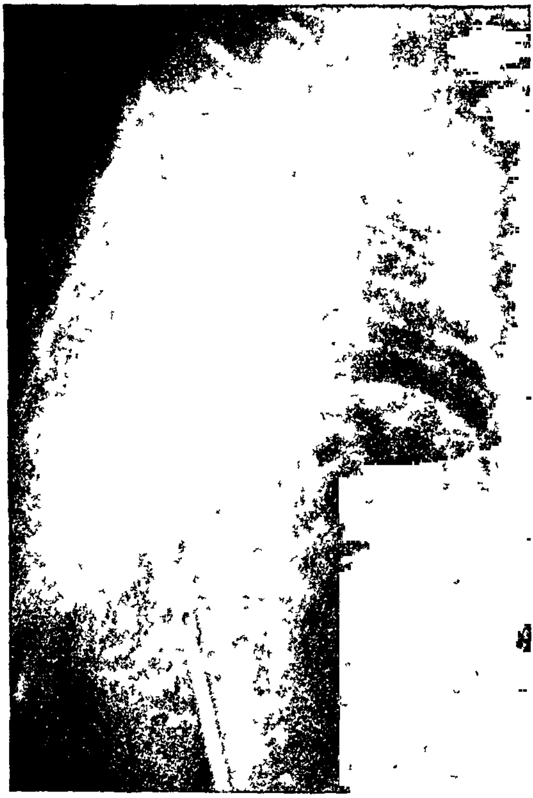

Fig 2

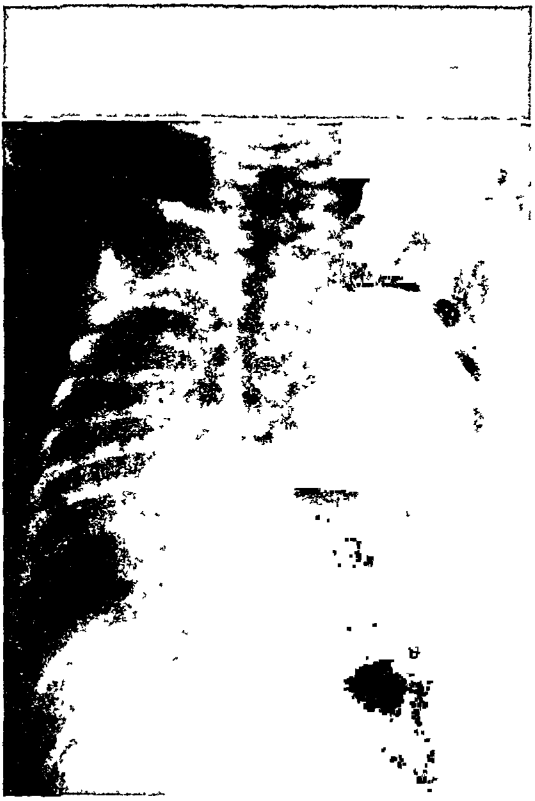

Fig 3

Fig. 2.—Chest roentgenogram made Nov. 24, 1958, immediately following removal of mediastinal teratoma

Fig 3 —Chest roentgenogram made on Dec 15, 1958. Heart remains shifted to the right. Left hemidiaphragm becoming progressively elevated.

During the first few postoperative days the infant breathed feebly, but the respiratory status improved thereafter. During the second postoperative week, however, the nurses noted occasional episodes of duskiness. Chest x-ray studies showed progressive elevation of the left hemidiaphragm (Fig. 3). By Dec. 24, 1958, the weight had dropped to 4 pounds, 9 ounces. The number of cyanotic spells had increased and the infant was showing considerable respiratory distress. The left hemithorax moved less than the right. The cardiac silhouette remained largely to the right. There was disagreement as to whether this represented persistent mediastinal shift or dextrocardia. The left diaphragm remained elevated and was motionless under fluoroscopy. An almost fatal episode of severe cyanosis and apnea resolved the period of indecision as to whether the infant should be subjected to surgery for correction of the elevated left diaphragm.

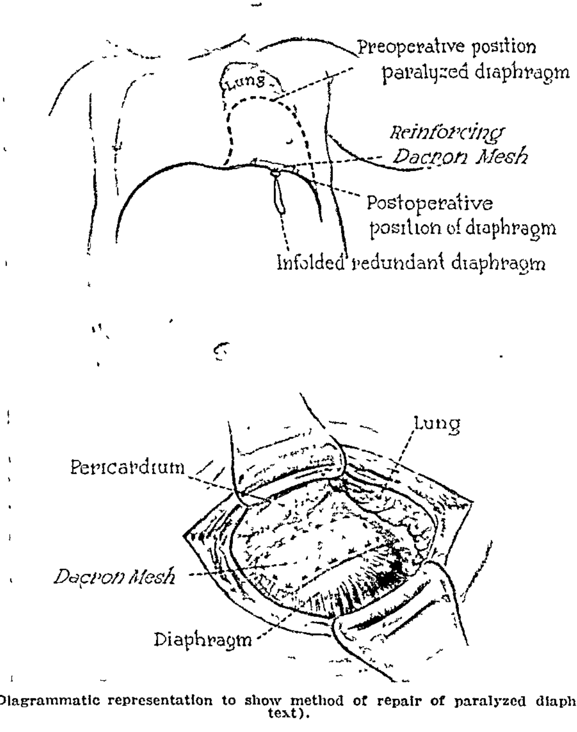

Fig. 4.—Diagrammatic representation to show method of repair of paralyzed diaphragm (see text).

On Dec. 27, 1958, thoracotomy was performed through the left seventh interspace. The elevated diaphragm filled the lower two thirds of the hemithorax. Adhesions between lung and diaphragm were divided and the dome of the diaphragm could then be depressed. The diaphragm was flaccid but it did not appear thin as with true eventration. The distal 2 cm. of the phrenic nerve, visible through this exposure, appeared normal. There was no response when stimulated by an electric current. The diaphragm muscle contracted weakly when electric current was applied directly to it. The redundant flaccid diaphragm was depressed inferiorly and the edges of the infolded area sutured together with interrupted silk leaving the diaphragm flat and tautly stretched between the costal attachments. The single suture line was reinforced by a patch of knitted Dacron mesh

(Fig. 4). This allowed the operation to be accomplished quickly and without need for exposing the abdominal contents through an opening in the diaphragm. The left lung was then freed from its costal adhesions, allowing it to expand inferiorly and fill the hemithorax down to the new low position of the diaphragm.

Postoperatively there was a dramatic change to a quiet regular type of respiration. The infant did well and gained weight. The last x-ray study before discharge showed the left hemidiaphragm in satisfactory position and the mediastinum returning to the left (Fig. 5). When last seen in April, 1959, she was an active healthy baby weighing 10 pounds.

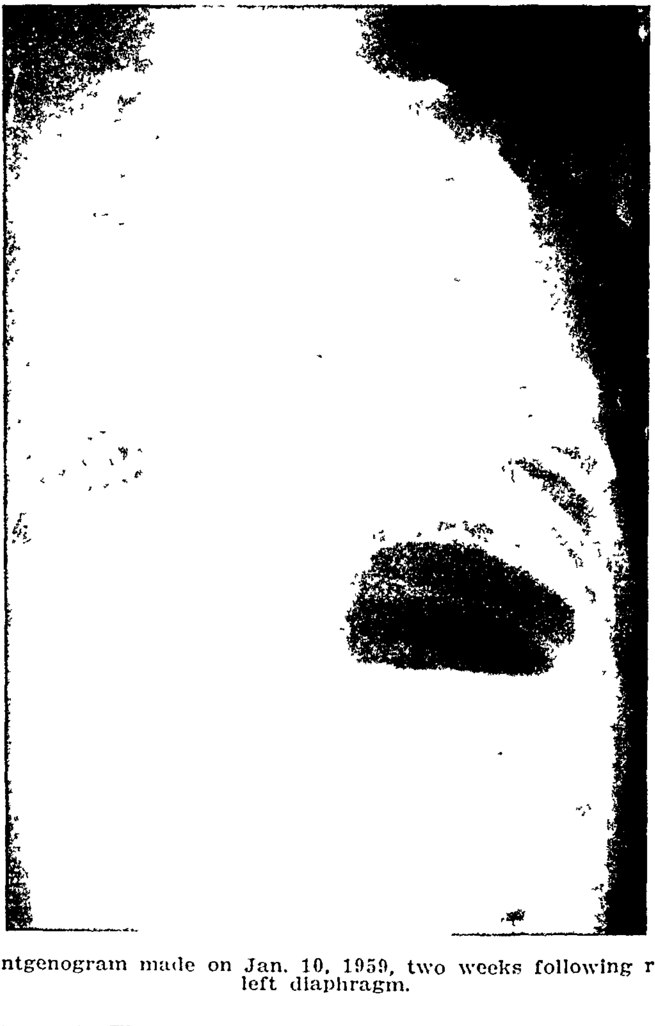

Fig. 5.—Chest roentgenogram made on Jan. 10, 1959, two weeks following repair of paralyzed left diaphragm.

*Pathologic Report.**—The teratoma was grossly a nodular, rounded tumor with a serous capsule, measuring 5.8 by 4.5 by 4.1 cm. as received in the frozen state. On the cut surface, the tumor had multiple cystic spaces containing mucoid- and colloid-like material (Fig. 6). Except for the more grayish-white color, the tumor resembled somewhat a colloid cystic goiter; neither bony nor epidermoid structures were seen.

Microscopically, this was a typical adult teratoma, consisting for the most part of derivatives of the entoderm with numerous glands and cysts lined by mucus-secreting epithelium. Groups of liver cells of varying size, and individual glands resembling bile ducts and pancreatic glands, were seen between the cysts. The intervening stroma contained markedly edematous mesenchymal structures, including numerous smooth muscle fibers, some fat tissue, and capillary vessels. Of particular interest, and somewhat outside of the general structural frame of this teratoma, was the finding of melanin pigment in the epithelial lining of two cysts, resembling the epithelium of the retina. The presence of this pigment points to some ectodermal analage. No undifferentiated or embryonal structures were seen. There was no anaplasia of any sort. Some cysts were lined by striated columnar epithelium resembling the mucosa of the respiratory tract.

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*Abstracted from the report by Dr. Kornel Terplan, Professor and Chairman of the Department of Pathology, University of Buffalo School of Medicine.

DISCUSSION

I. *Mediastinal Teratoma.*—Today most authorities prefer to erase the earlier idea of a distinction between mediastinal dermoid cysts and teratomas because of the frequency with which teratomatous elements can be demonstrated when dermoid cysts are subjected to comprehensive examination. These lesions may be collectively called teratoid tumors or else referred to as cystic and solid teratomas. Cystic teratomas outnumber the solid ones. The solid tumors are more complex, however, and have a greater propensity for malignant change. The incidence of malignancy for both types has been quoted as from 10 to 33 per cent, but a figure around 20 per cent would appear to be an acceptable average.

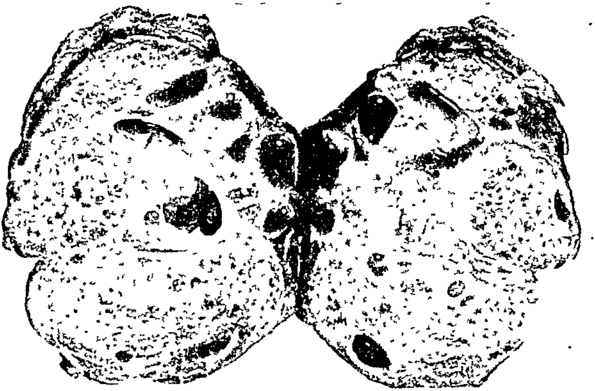
FIG. 6—Gross appearance of mediastinal teratoma (cut section)

The etiology of teratomas has been a subject for considerable speculation, but no single opinion is as yet universally accepted. Perhaps the most plausible theory of the genesis of extragonadal teratomas is that they are the result of local dislocation of tissue during embryogenesis. In discussing mediastinal teratomas, Schlumberger[21] incriminates the branchial clefts, specifically tissue dislocations in the anlage of the thymus. It has been stated that the thymus is the only branchiogenic structure to descend routinely into the mediastinum and also one that may give rise to derivatives of all three germinal layers. The close association with the thymus would also explain in part why most teratomas occur in the anterior mediastinum.

It is generally stated that there is no appreciable difference in the sex incidences of these tumors. Ochsner,[18] however, has said that in children there is a great preponderance of females. Although many tumors are asymptomatic at the time of discovery, the majority will eventually give rise to symptoms and contribute to the death of the individual.[22] The tumors usually cause symptoms because of pressure on or erosion into nearby structures. Less commonly, the individual may cough up hair or other suspicious material. Occasionally, a cystic lesion may become infected and perforate into the lung or pleura. In general, the tumors grow slowly and remain asymptomatic for years. It has been suggested that some teratomas receive a growth stimulus around the time of puberty. With malignant change, however, the growth process may be greatly accelerated.

The tumors are usually discovered between the ages of 20 to 40 years, either because of symptoms or, commonly, as a result of routine roentgenograms of the chest in an asymptomatic individual. Most published series on mediastinal teratomas concern adults with little or no mention of its occurrence in infants and young children. With few exceptions,[7, 10] the reports on mediastinal teratomas in infants have consisted mostly of single case reports. In several papers published about the turn of this century, it is difficult to determine whether the lesions were teratoid tumors or bronchogenic, enterogenous, or other types of cystic and solid malformations. A few reports dealing with the broader subject of mediastinal tumors and teratomas refer to infants or young children only by stating the oldest and youngest subject in the series or else by general age grouping, listing the number under 20 years or 12 years of age. It becomes apparent, therefore, that it is not possible to state an absolute figure as to the number of mediastinal teratomas found in infancy in the literature. Nevertheless, it is of interest to review briefly the available literature on mediastinal teratomas in infancy.

Approximately 26 extrapericardial teratomas occurring in infancy have been found in our review of the literature. In this connection, infancy has been taken as a period under 2 years of age. Because of incomplete documentation in two collective reviews, it is possible that several references to a few early cases may overlap (Table I).

TABLE I. MEDIASTINAL TERATOMAS OF INFANCY

AUTHORS AND DATES	NO. PATIENTS	AGES	COMMENTS
Kerr and Warfield,[16] 1928	3	First year of life	Literature review
Poynton,[20] 1929	1	4 mo.	Autopsy; no operation
Wilcox and Wollstein,[29] 1931	1	6 mo.	Autopsy; no operation
Struthers,[26] 1932	1	5 mo.	Autopsy; no operation
Hedblom,[11] 1933	6	3-8 mo.	Collective review
Rusby,[22] 1944	1	16 mo.	Autopsy; malignant teratoma
Laipply,[17] 1945	1	"Stillborn"	No details
Total	14		

With one exception,[28] the 12 infants with mediastinal teratomas surgically removed have been reported during the past decade (Table II).

TABLE II MEDIASTINAL TERATOMAS OF INFANCY

AUTHORS AND DATES	NO PATIENTS	AGES	COMMENTS
Wheatley,[28] 1937	1	7 mo	Died following surgery
Vervat,[27] 1949	1	8 mo	Successfully removed
Gross,[10] 1953	3	2, 19, 21 mo	Successfully removed
Starer,[25] 1954	1	10 da	Successfully removed
Sarinana et al.,[23] 1954	1	2 mo	Successfully removed
Peabody et al.[19] 1954	1	4 mo	Successfully removed
Ellis et al.,[7] 1955	3	3 wk., 3, 5 mo	Successfully removed
Herlitzka and Gale[illegible] 1958	1	3 mo	No details
Total	12		

A word should be included about the so-called intrapericardial teratomas. Actually these tumors are also mediastinal and some have considered them to be similar to the more common anterior mediastinal extrapericardial teratomas with a chance location inside rather than outside the pericardium. It is of interest that most of these tumors have been found in infancy or childhood in contrast to the extrapericardial mediastinal teratomas which are usually found in adults. It may be that the intrapericardial tumors become apparent at an earlier age because they are contained in closer proximity to the heart and great vessels and even a small tumor mass may give rise to noticeable signs and symptoms. A review of the literature revealed nine intrapericardial teratomas, six occurring in infancy (Table III).

TABLE III INTRAPERICARDIAL MEDIASTINAL TERATOMAS

AUTHORS AND DATES	NO PATIENTS	AGES	COMMENTS
Grimm,[9] 1927	1	3 mo	Died, no surgery
Jellen and Fisher,[14] 1936	1	3 wk.	Died, no surgery
Willis,[30] 1946	1	10 wk.	Died, no surgery
Claireaux,[6] 1951	1	Premature newborn	Died, no surgery
Basora, Defillo and Lichtenberg,[3] 1956	1	15 da	Died, no surgery
Richards and Reeves,[21] 1958	1	3 mo	Successfully removed
		Children and Adults	
Joel,[15] 1890	1	14 yr	No details
Beck,[4] 1942	1	22 yr	Successfully removed
Gebauer,[8] 1943	1	12 year	Died, hemorrhage at surgery
Total	9		

The intimate association of intrapericardial teratomas with the heart or great vessel becomes of great practical importance when such tumors are to be surgically removed. This was dramatically shown in the report of Gebauer[8] in which fatal hemorrhage occurred when the first portion of the aorta was inadvertently perforated while attempting to remove an intrapericardial teratoma, adherent to this site, in a 12 year old girl. In a number of autopsy dissections, the intrapericardial teratoma has been described as attached to the adventitia of the great vessels by a stalk which would have presented a less hazardous technical problem at surgery.

It seems reasonable to assume that most if not all mediastinal teratomas are present at birth. The true incidence of this tumor in infancy might be more accurately appraised if all infants were subjected to routine chest x-ray studies. Unless special projections were taken, however, small tumors might be missed at this early age with a routine posteroanterior chest film as taken in adult surveys. Certainly one would not recommend unnecessary x-ray exposure to normal asymptomatic infants merely in an effort to detect a mediastinal teratoma.

Practically all mediastinal teratomas in infancy have been found because they caused signs and symptoms or else they were discovered at postmortem examination. Cough, dyspnea, and cyanotic episodes are the predominant symptoms in infants. Other findings are occasionally encountered as a result of pressure, perforation, or infection. With large tumors filling the hemithorax, the involved side may lag with respiration and show protruding intercostal spaces. The percussion note will be flat with diminished breath sounds and the displaced maximum cardiac impulse may reflect a mediastinal shift. A roentgenogram of the chest will usually show a dense rounded mass with sharply defined borders projecting laterally into either hemithorax and blending centrally with a mediastinal cardiac shadow, usually located in the anterior mediastinum. If the mass contains plaques of calcium or a tooth, the diagnosis becomes quite certain.

Unless the tumor is intimately adherent to the heart or aorta, as with intrapericardial teratomas, the mass is frequently well circumscribed and easily shelled out from its surroundings at operation. With infection, perforation, or malignant degeneration, complete removal may be difficult or impossible. Certain diagnostic and therapeutic procedures used before the development of modern thoracic surgery, such as needle aspirations, drainage and decompression, and marsupialization will rarely be indicated. Once the lesion has been demonstrated it should be excised to relieve symptoms and to avoid further complications and malignant degeneration.

Various derivatives of all three germ layers may be found in these tumors. Of interest is the finding of pancreas and thymus in a considerable number of the more solid tumors.[13] The case presented in this paper had pancreas in the teratoma but it was free of any thymic tissue. There was no connection with the thymus gland.

II. *Paralyzed Left Hemidiaphragm.*—There were no signs of brachial plexus injury or other evidence to suggest that a birth injury could have been the cause of the paralyzed diaphragm, a so-called acquired eventration. Although the diaphragm appeared to be near normal position immediately following removal of the tumor, it became progressively elevated during the following 4 weeks causing increasing respiratory disturbance. In this case, the most probable cause of the paralyzed diaphragm would appear to have been inadvertent trauma to the phrenic nerve during removal of the teratoma. In retrospect, the paralyzed diaphragm should have been repaired by surgery earlier.

Disappearance of the severe dyspnea following operative return of the left hemidiaphragm to a lowered position was quite dramatic. The left lung could not fully expand to fill the space that had been occupied by the elevated hemidiaphragm until adhesions between lung and chest wall as a result of previous thoracotomy, were separated. The lung then expanded easily to fill the entire left hemithorax. The infant breathed normally thereafter, although the diaphragm remained motionless.

In discussing eventration of the diaphragm in infancy, Bishop and Koop[3] recently emphasized the relief of respiratory distress that follows the lowering of a paralyzed diaphragm. These authors recommend excising a generous full thickness ellipse from the central area of the diaphragm and imbricating the free edges. Others have used plication, especially in true eventration presenting a thin or atropic diaphragm, without incising the diaphragm. We decided against opening the diaphragm because of the extra time required for hemostasis and suturing in this critically dyspneic infant. It also eliminated the necessity of depressing abdominal viscera that might tend to herniate upward, as well as reduce the possibility of accidental injury to the spleen.

A low thoracotomy approach allowed proper inversion of the elevated diaphragm resulting in a central fold where the redundant dome was depressed into the abdomen. A row of interrupted sutures quickly placed, held the diaphragm in this flattened, depressed position. The suture line was then reinforced by suturing a patch of knitted Dacron mesh to the diaphragm around this area. Our experience with this form of pliable synthetic mesh for reinforcing tissue deficiencies of the diaphragm has been most satisfactory to date.[1, 2] Admittedly, this also could have been repaired by imbricating the redundant muscular diaphragm dome which might have added a little extra intrathoracic bulk at the diaphragm level. The point to be stressed, however, is the need for recognizing that severe respiratory distress may be associated with a paralyzed diaphragm in infancy and that the condition may be effectively corrected by a relatively simple operative procedure of lowering the elevated diaphragm.

SUMMARY

1. A large mediastinal teratoma was successfully removed from a premature infant 2 days after birth.

2. A paralyzed left diaphragm (acquired eventration) was repaired several weeks after the teratoma had been removed by using a reinforcing patch of knitted Dacron mesh. Dyspnea dramatically disappeared following repair of the elevated diaphragm.

3. The literature on mediastinal teratoma in infancy, both inside and outside the pericardium, is reviewed. Points of interest from this case and the literature are discussed.

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RESECTIONAL THERAPY FOR PULMONARY TUBERCULOSIS AT SUNMOUNT, 1950-1957, 807 CASES

III. An Evaluation of the Technique of Reconstitution of the Lung in Segmental Resections

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THE PROBLEM of what to do with the raw surfaces of the lung after a segmental resection is still a matter of some controversy. In 1956, Dr. Bell[1] reviewed the different thoughts on this subject and, at the same time, described his technique of reconstitution of the lung.

By reconstitution is meant the approximation of raw surfaces, the obliteration of intrapulmonary dead space, and the burying of the bronchial stump in lung tissue. As a result, no raw surfaces, but only pleural surfaces are allowed to come in contact with the parietal pleura. It was Dr. Bell's clinical impression that the incidence of postoperative complications, especially space problems, was significantly reduced when the method of reconstitution was used.

To evaluate this clinical impression critically, segmental resections and segmental resections with concomitant wedge resections done at Sunmount between the years 1950 to 1957, inclusive, were studied. During this 8 year period, a total of 348 segmental resections and segmental resections with concomitant wedge resection were performed for pulmonary tuberculosis. In 125 cases, the method of reconstitution, as described by Dr. Bell, was applied. In the other 223 cases, the raw surfaces of the lung were not covered, but were allowed, on expansion, to come in contact with the parietal pleura, and to "seal themselves." The incidence of major and minor complications for these two groups of cases was determined. Table I lists the incidence of space problems and major complications in the presence and absence of reconstitution. Major complications include empyema, fistula, and occult fistula. The difference in the major complication rate in the two groups, 12.1 per cent versus 2.4 per cent, is noteworthy. There were no deaths in the group of patients who had segmental resections with reconstitution, and three deaths in the other group. One of these deaths occurred 3½ months postoperatively when an occult fistula eroded into a pulmonary artery. A second death occurred postoperatively from a bleeding diathesis. The third death occurred 4 days postoperatively from cardiac

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arrest, which was probably precipitated by massive subcutaneous emphysema and air leak which persisted despite complete expansion of the lung according to x-ray evidence. The latter 2 cases are not included under the major complications as defined above. Their addition would raise the total number of serious complications to 29, or 13 per cent.

TABLE I. COMPLICATIONS IN SEGMENTAL RESECTIONS AND SEGMENTAL AND WEDGE RESECTIONS, WITH AND WITHOUT RECONSTITUTION

	POSTOP. SPACE PROBLEMS	MAJOR COMPLICATIONS	OPERATIVE DEATHS
Segmental resections with reconstitution 125 Cases	38 (30%)	3 (2.4%)	0
Segmental resections without reconstitution 223 Cases	107 (48%)	27 (12%)	3 (1.3%)

The difference in the incidence of space problems in the two groups, 48 per cent versus 30 per cent, does not appear too striking on superficial examination. But if we divide the postoperative space problems into three categories in an attempt to grade the morbidity, the differences become more pronounced. In Table II postoperative space problems have been divided into three categories: (1) spaces which require no further therapy and disappear spontaneously, (2) spaces which require relatively minor additional treatment, namely, intubation, and (3) spaces which require thoracoplastics. The incidence of spaces requiring no additional treatment is the same in the two groups; but space problems which required additional treatment occurred three and a half times more often when reconstitution was not carried out.

TABLE II. SPACE PROBLEMS IN SEGMENTAL RESECTIONS AND SEGMENTAL AND WEDGE RESECTIONS, WITH AND WITHOUT RECONSTITUTION

	SPACE REQUIRING NO SPECIFIC RX	SPACE REQUIRING INTUBATION	SPACE REQUIRING THORACOPLASTY
Segmental resections with reconstitution 125 Cases	30 (24%)	8 (6.4%)	0
Segmental resections without reconstitution 223 Cases	55 (25%)	47 (21%)	5 (2%)

Since it was a frequent practice at this hospital during the early days of wedge resections to allow raw lung surface to remain after simple wedge resections, it was thought desirable also to study a group of pure segmental resections. By eliminating those cases in which a wedge resection accompanied a segmental resection, the group for evaluation was reduced to 193 cases. In this group, 85 cases represent segmental resections with reconstitution, and 108 cases segmental resections without reconstitution. In Table III the incidence of space problems, space problems requiring treatment, and major complications for the group of pure segmental resections is summarized. The findings here are entirely comparable with those in the larger group which includes concomitant wedge resections.

TABLE III COMPLICATIONS AND SPACE PROBLEMS IN PURE SEGMENTAL RESECTIONS, WITH AND WITHOUT RECONSTITUTION

	SPACE REQUIRING NO SPECIFIC THERAPY	SPACE REQUIRING INTUBATION	SPACE REQUIRING THORACOPLASTY	MAJOR COMPLICATIONS
Segmental resections with reconstitution 85 Cases	16 (19%)	5 (6%)	0	2 (2.4%)
Segmental resections without reconstitution 108 Cases	29 (27%)	21 (19%)	1 (0.9%)	16 (15%)

DISCUSSION

The above figures clearly indicate that the incidence of space problems, especially serious space problems, and major complications is significantly less when reconstitution is carried out. The fact that the incidence of space problems which require no additional treatment in the two groups of cases is approximately the same suggests that the mechanics of filling space, namely, expansion and shift, are not significantly altered by the technical maneuver of reconstitution. However, the greater incidence of space problems requiring additional treatment in the group without reconstitution suggests that significant trouble some postoperative air leaks are minimized by the technique of reconstitution.

One may now question whether the two groups are comparable in other respects. The anatomic location and number of segments removed in the two groups have been analyzed and found to be completely comparable. It was also found that the extent of the resection did not correlate with either major complications or space problems. As the majority of resections without reconstitution was carried out prior to 1954, there may exist some difference in the chemotherapy coverage available. With this point in mind, chemotherapy coverage in the complications was evaluated. Chemotherapy coverage was graded as good and poor, as defined elsewhere[2]. It was found that 50 per cent of the patients with major complications in the non reconstitution group had good chemotherapy coverage. Empyemas in this group were nontuberculous by culture. Surprisingly, a large number of patients who had complications while on poor chemotherapy coverage also had nontuberculous empyemas by culture and no subsequent evidence of active tuberculosis. Of the three complications in the group of segmental resections with reconstitution, 2 patients had poor drug coverage, and one patient had good chemotherapy.

The high incidence (50 per cent) of patients with good chemotherapy coverage and complications in the group without reconstitution, and the fact that ten of thirteen empyemas in that group failed to culture tuberculous organisms, strongly suggests that the complications encountered are frequently not due to underlying tuberculosis. These data strongly suggest that the combination of contamination from air leak plus a convenient culture medium supplied by raw lung surface are the offenders.

The complications in the group with reconstitution consisted of two non tuberculous empyemas and an occult fistula in a patient with poor chemotherapy coverage. Seven occult fistulas are included among the twenty-seven major complications for the combined segmental and wedge resections without reconstitution, while the sixteen major complications in the pure segmental resections without reconstitution include five occult fistulas.

SUMMARY

1. One hundred and twenty-five combined segmental and wedge resections with reconstitution, and a similar group of 223 cases without reconstitution have been analyzed as to postoperative complications as determined by the incidence of space problems, fistulas, empyemas, and occult fistulas. A smaller group of pure segmental resections has been similarly studied.

2. It has been shown that there is a significantly higher incidence of major complications and space problems in segmental resections without reconstitution.

3. A large percentage of the complications encountered occurred in the presence of good chemotherapy coverage and were due to infection with secondary organisms.

4. The conclusion is drawn that the anatomic situation, comprising the conical segmental defect with raw lung surface exposed to pleural cavity, plus secondary, contamination from air leaks, is favorable to the development of secondary infections and should therefore be avoided.

5. Reconstitution of raw lung surfaces presents a method of avoiding the undesirable anatomic situation, of reducing serious air leaks and, therefore, markedly reduces the incidence of serious postoperative complications.

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BRONCHOGENIC CARCINOMA: COMPARISON OF NATURAL COURSE AND TREATMENT WITH RESECTION, X-RADIATION, AND NITROGEN MUSTARD

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THIS is a report of a group of 547 consecutive proved bronchogenic carcinomas in patients who have all been followed for 6 months to 12 years. This series is unusual because the 30 day mortality after resection was less than 3 per cent, because lobectomy was almost as frequent as pneumonectomy, and because 37 per cent of the patients subjected to resection and over 10 per cent of all patients were alive 5 years after proved diagnosis. Meade and co-workers,[1] in 1946, reported the experiences with lobectomy from one of the Army's larger chest surgical centers and this service has been continued by the Veterans Administration at Kennedy Hospital. The authors believe that this extensive background of chest specialization and continuation of full time interest is responsible for this series of patients.

TABLE I. PRESENTING SYMPTOMS

SYMPTOM	DURATION BEFORE HOSPITALIZATION			
	PER CENT OF CASES	0 TO 3 MO (%)	MORE THAN 24 MO (%)	AVERAGE (MO.)
Cough	65.2	35.8	18.5	7.8
Gross bleeding	35.6	29.9	21.8	11.0
Chest pain	37.1	38.4	13.7	8.6
Weight loss	34.4	36.0	12.8	7.7
Dyspnea	24.6	33.9	26.0	11.6
Fever	11.6	48.3	8.3	9.9
Weakness	8.1	52.4	9.5	6.7
Routine x-ray	7.3	—	—	—
Joint pains	7.0	—	—	—
Hoarseness	5.0	—	—	—
Pneumonia	5.0	—	—	—
Palpable masses	4.0	—	—	—
Back pain	3.0	—	—	—
Wheezing	3.0	—	—	—

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DIAGNOSIS

The occurrence of various presenting symptoms is shown in Table I. Over 60 per cent of the group experienced symptoms more than 3 months before hospitalization.

Twenty-one per cent of the patients showed no abnormalities on physical examination at the time of admission. An additional 34 per cent showed no significant abnormalities outside the chest.

The admission x-ray findings are reported in Table II. Only 7 per cent of the lesions were less than 3 cm. in diameter, and 73 per cent were over 6 cm. in diameter.

TABLE II. X-RAY FINDINGS ON ADMISSION (523 CASES)

			NUMBER	PER CENT
Mass in lung			222	42.4
(a) Multiple	20	3.8%		
(b) "Pancoasts"	8	1.5%		
Hilar mass			115	22.0
"Soft" infiltrates			84	16.1
Atelectasis			62	11.9
Effusion			52	9.9
Rib erosion			27	5.2
Cavity in lung			22	4.2
Negative			19	3.6
Emphysema, only			16	3.1
[illegible] ion			15	2.9
[illegible]			6	1.1
Spine erosion, only			3	0.6

The diagnosis was proved by surgery in 38 per cent, by bronchoscopy in 29 per cent, at autopsy in 20 per cent (not suspected prior to death in 6 per cent), and by supraclavicular node dissection in 13 per cent.

Supraclavicular node dissections were performed on more than 100 patients, but gave histologic proof of cancer in only 20 per cent of these cases. When palpable nodes were absent, the procedure was of little help in making the diagnosis.

Cytologic examination of the sputum was disappointing as a diagnostic aid during its first few years of use. However, analysis of the results in the last 2 years reveals 81 per cent accuracy with only 4 per cent false positives.

It was difficult, in many cases, to differentiate a metastic cancer from a primary bronchogenic carcinoma. In 15 cases in which a diagnosis of metastatic tumor was made, autopsy revealed the pulmonary mass to be a primary bronchogenic carcinoma. In 20 additional cases, the clinical diagnosis of tuberculosis, pneumonia, or brain tumor was proved by autopsy to be bronchogenic cancer.

SELECTION FOR SURGERY

The most important factor affecting the operative mortality rate and 5-year survival is the selection of patients for surgery with localized or relatively controlled cancer.

A 1- to 2 week period of observation allows many suspected cases to be excluded from surgery due to clearing of the lesion or to detection of previously obscure metastasis After cancer has metastasized, any surgical procedure is usually futile, offers false hope to the patient and family, and is unnecessarily derogatory of definitive surgery due to the associated high operative mortality rate or early death of the patient

We have consistently recommended resection of pulmonary lesions after failure of diagnosis or medical therapy This has resulted in many cases, in the removal of very early tumors Several lobes removed for chronic inflammatory disease have revealed carcinoma, almost of the in situ type

Contraindications to surgery included obviously terminal cases (15 4 per cent), distant metastases (23 9 per cent), local extension (16 6 per cent), to heart, brachial plexus, ribs, trachea (1 8 per cent), and diaphragm (1 3 per cent), or malignant effusions (2 2 per cent) A few patients refused surgery (0 9 per cent)

Tumor invasion of the left recurrent nerve or either phrenic nerve was present in some patients in whom the lesion remained localized to an area which could be completely resected Occasionally, these patients survived over 5 years

Realization that surgery offered a fair hope of cure and a low mortality led to broadening the criteria for operation and a willingness to offer resection to all patients without clear cut evidence of incurability Forty one per cent of all patients were operated upon

SURGERY

One hundred thirty seven patients had pulmonary resections (60 3 per cent of the operated cases, 25 per cent of all cases) Squamous carcinomas were found the most likely to be resectable, and alveolar cell carcinomas least likely (Table III) We prefer to perform resections in all cases possible since it is not apparent from clinical studies which patients may be cured and which will obtain only palliation

TABLE III HISTOLOGY

CELL TYPE	NUMBER OF CASES	PER CENT TOTAL CASES	PER CENT OPERABLE	PER CENT RESECTABLE	5 YEAR SURVIVAL	
					RESECTED CASES	ALL CASES
Anaplastic	193	35 3	42 5	46	21	(4/74) 5 4
Squamous	169	30 9	39 4	78	42	(10/70) 14 3
Poorly differentiated bronchogenic	120	21 9	34 0	66	47	(7/81) 8 6
Adenocarcinoma	55	10 1	58 0	50	30	(3/40) 7 5
Alveolar	10	1 8	40 0	20	0	(0/2) 0 0
Totals	547	100	41 1	60	37	(24/267) 9 0

After lobectomy or pneumonectomy, the mediastinum is now dissected and all obvious lymph nodes removed, but this was not always done Intrapericardial dissection of the vessels was frequent, although not routine Lobectomy has

TABLE IV

TREATMENT	ALL CASES				CASES SEEN OVER FIVE YEARS AGO			
	NUMBER OF CASES	NUMBER ALIVE	PER CENT ALIVE	MEAN FOLLOW-UP MO.	NUMBER OF CASES	NO. ALIVE MORE THAN 5 YEARS	PER CENT ALIVE MORE THAN 5 YEARS	MEAN SURVIVAL OF PATIENTS WHO DIED IN LESS THAN 5 YR.
*Pneumonectomies**								
Curative	32	14	44	54.1	19	11	58	13.7
Palliative	23	17	74	29.0	18	3	17	11.6
Totals	55	31	56	43.7	37	14	38	12.5
*Lobectomies**								
Curative	18	11	61	41.6	8	6	75	14.7
Palliative	27	4	15	9.5	14	2	14	13.0
Totals*	45	15	33	33.7	22	8	36	13.7
Segmental	2	0	0	—	2	0	0	28.0
Exploratory only	17	0	0	0.0	9	0	0	3.8
Exploratory plus x-ray and/or mustard	73	8	11	23.0	43	1	2	11.6
Totals	90	8	9	23.0	52	1	2	8.2
Nitrogen mustard	21	2	9.5	4.1	5	0	0	7.4
X-ray	161	20	12	12.6	73	0	0	9.4
X-ray and mustard	30	2	7	18.7	8	0	0	8.1
No treatment	108	0	0	81.0	68	1	1	6.9
Totals	320	24	7.5	29.0	154	1	.3	7.9
Grand totals	512	78	15.2		267	24	9.0	8.3

*Pulmonary resections performed elsewhere but with the patients treated here later are *not* included.

been consistently preferred because of the marked disability noted in healthy young patients subjected to pneumonectomy before 1945. Our results following lobectomy done before 1952 were good (36 per cent 5 year survival). This finding led us to extend the indications for lobectomy in the next 2 years with a marked drop in the survival rate.

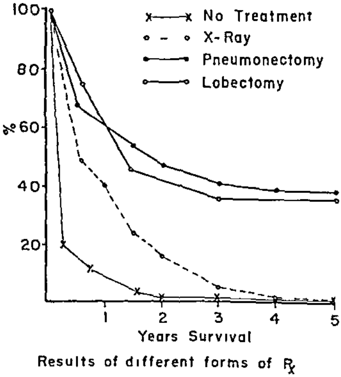

Fig 1.—Results of various forms of treatment in improving the prognosis of patients with cancer of the lung.

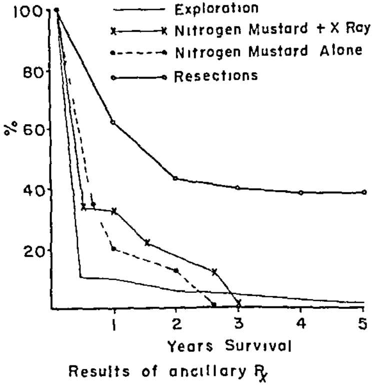

Fig 2.—Survival of patients receiving different forms of treatment.

The operating room mortality was 1.8 per cent for pneumonectomy (0 in the last 10 years) and 0 per cent for lobectomy. No other patient having pneumonectomy died within 30 days of surgery, but 2 of those having lobectomy died. The causes of death were metastatic cancer and cerebrovascular accident

ANCILLARY THERAPY (Figs. 1 and 2)

If there was doubt of complete removal of all tumor by the resection, nitrogen mustard and/or x-radiation was also given. These agents were given to 23 patients (42 per cent) having pneumonectomy and to 27 patients (60 per cent) having lobectomy on our service.

We are currently in a cooperative study on the effects of simultaneous chemotherapy and surgery. None of the cases placed on these protocols has been included in this report.

Of the patients explored without resection, 73 (81 per cent) received x-radiation mustard therapy or both. There was apparently some favorable effect from these agents in this group.

One hundred and eight patients (19.7 per cent) were given no specific cancer therapy. This group included a few patients who refused all aid, as well as the obviously terminal cases.

When cure is not possible, we employ an aggresive approach aimed at giving a maximum enjoyment of remaining life. Tranquilizers, adequate feeding, x-radiation, and chemotherapy are used to the maximal extent and as often as possible. These agents are not withheld until needed for pain control.

RESULTS

Survival time (Figs. 1 and 2, and Table IV) was considered to be from the time of original admission to the hospital to death, unless the patient was operated upon, in which case it was from the day of surgery to death.

"Curative" resections are those in which the staff did not use x-radiation or nitrogen mustard within the first 3 months following surgery, and "palliative" are those who were given x-radiation or nitrogen mustard during the postoperative period. The decision to use x-radiation therapy is based on many factors, such as the microscopic appearance of the lymph nodes, proximity of tumor to lines of resection, invasion of vessels, etc.

It is apparent that in those cases in which x-radiation and/or mustard therapy was selected, the choice was appropriate, since the 5-year survival rate was only about 15 per cent as opposed to the 63 per cent rate in those cases in which these agents were not employed. Of course, metastases which became apparent and were treated within 3 months of surgery could bias these data in favor of the "curative" resections. While this did occur, it was not common.

It is possible to obtain as satisfactory results with lobectomy as with pneumonectomy in properly selected cases.

Factors which influenced the decision to do a lobectomy included: absence of involvement of primary or intermediate bronchi, main pulmonary artery, or fissure; peripheral location, particularly in the upper lobes; and poor pulmonary reserve (by clinical estimation).

Table IV shows that exploration followed by x-radiation and/or nitrogen mustard therapy gave results which were better than no treatment and in the same range as x-ray therapy alone.

Nitrogen mustard has been used in 96 cases in this group: in 21 as the sole therapy, in 30 in conjunction with x-ray therapy, in 21 of exploration, and in 24 of resection The survival data do not reveal an effect from the drug however, our clinical feeling is quite the contrary In a few incidences, the response to nitrogen mustard has been gratifying

X-ray therapy was used as the sole specific treatment in 161 cases and in conjunction with other modes of therapy in 166 additional cases for a total of 327 cases (73 per cent of the series) When used alone the 5 year survival rate was 0 and the mean survival time was only 9 4 months However (Fig 1), x ray therapy offers a clear cut increase in the probability of living between 1 and 2 years, aside from palliation

Since many of our patients were transferred to us from other hospitals and these data are biased due to referral for terminal care or x radiation therapy, we have made a separate analysis of patients who were admitted first to our hospital

Results in Kennedy Patients—Excluding the 53 cases transferred here for terminal care, and the 67 patients operated upon elsewhere before referral there remained 427 patients who were either available for therapy or were seen for the first admission at our hospital Of these 427 cases, 209 were admitted over 5 years ago

In 136 cases there was no evidence of extension or metastasis at the time of entering the hospital Twenty three of these patients were alive 5 years after admission This gives a 5 year survival rate of 16 9 per cent for those patients admitted before obvious signs and symptoms of extension or metastasis had become apparent The 5 year survival rate of *all* patients admitted originally to this hospital is 11 5 per cent (24/209)

We have complete information in 371 cases as to sites of extension The parietal pleura was invaded by direct extension in 59 cases (15 9 per cent) The ribs were involved in 43 patients (11 6 per cent), pericardium in 28 (7 5 per cent), other lung in 3 5 per cent, heart in 2 7 per cent, superior vena cava in 1 9 per cent, aorta in 1 9 per cent, and esophagus in 1 3 per cent

Sites of metastasis are shown in Table V It is seen that the retroperitoneal structures, i e , adrenals, liver, kidneys, and pancreas, were frequently involved This may be accounted for by the direct lymphatic connections from the lung to this region The high rate of involvement of the adrenals should always be kept in mind when shock persists after surgery Practically no structure in the body is immune to metastatic implants

TABLE V SITES OF METASTASIS (274 COMPLETE AUTOPSIES)

	NO OF CASES	PER CENT		NO OF CASES	PER CENT
Mediastinal nodes	157	57 3			
Adrenals	113	41 2	Spleen	34	12 4
Bone	101	36 9	Gut	25	9 1
Liver	89	32 5	Thyroid	18	6 6
Kidney	63	23 0	Skin	14	5 1
Lung	58	21 2	Prostate	4	1 5
Brain	50	18 2	Gall bladder	3	1 1
Heart	43	15 7	Pituitary	3	1 1
None	37	13 5	Bladder	1	0 4
Pancreas	36	13 1	Testis	1	0 4

SUMMARY

1. Five hundred forty-seven consecutive proved cases of bronchogenic carcinoma with follow-up of all patients are analyzed. The median age was 58 years.

2. The average duration of symptoms before hospitalization was over 8 months, and 16 per cent of the patients had symptoms over 2 years before being admitted. Seven per cent of the patients had abnormal routine chest x-ray studies in the absence of symptoms; 65 per cent had a mass demonstrated on roentgenograms of the chest, and these masses exceeded 6 cm. in diameter in 73 per cent of cases.

3. The operability rate was 41.4 per cent of all patients admitted; the resectability rate was 60.3 per cent of those patients operated upon.

4. Lobectomy *in properly selected cases* gave results comparable to pneumonectomy. The operating room mortality was less than 1 per cent, and the 30-day mortality slightly over 2 per cent.

5. The 5-year survival rate after resection was 37 per cent.

6. High voltage x-radiation and nitrogen mustard therapy earned a place in prolonging useful life and in palliation.

7. The 5-year survival rate of *all* patients with bronchogenic carcinoma originally admitted to this hospital was 11.5 per cent (24/209).

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PERFORMANCE OF THE STATIONARY VERTICAL-SCREEN OXYGENATOR (MAYO-GIBBON)

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Some general information on the transfer of oxygen in the stationary vertical-screen oxygenator (Mayo-Gibbon) with blood flowing at rates of 160 to 260 ml. per minute per screen has been published.[1] The present study confirms the previous impression that the performance of this apparatus is reproducible and indicates further that oxygen transfer is related to the amount of reduced hemoglobin entering the oxygenator.

METHODS

Oxygen tension in blood was measured by a polarographic method using the Clark oxygen electrode.[2] The electrodes were calibrated at the temperature observed at the electrode during the perfusion. Three calibration points were obtained, and a calibration line for each electrode was constructed.

The oxygen content, oxygen capacity, and carbon dioxide content of the blood were determined according to the method of Van Slyke and Neill.[3] The amount of hemoglobin was calculated by dividing the corrected oxygen

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capacity[4] by 1.34. The amount of dissolved oxygen was calculated in Cases 1 through 10 from the oxygen tension observed at the appropriate oxygen electrode and the solubility coefficient for whole blood (0.023 ml. [STPD] of oxygen per milliliter of solution at an oxygen pressure [pO_2] of 760 mm. Hg at 37° C.).[4] In Cases 11 through 17, the amount of dissolved oxygen was assumed to be 0.1 and 0.3 volume per cent, respectively, in samples obtained from blood entering and leaving the oxygenator. The amount of oxyhemoglobin was calculated by subtracting the amount of dissolved oxygen from the total oxygen content and dividing the remainder by 1.34. The percentage saturation of hemoglobin with oxygen was calculated as 100 × (concentration of oxyhemoglobin ÷ concentration of total hemoglobin). The amount of reduced hemoglobin was obtained by subtracting the oxyhemoglobin content from the total hemoglobin content. The amount of oxygen added per screen was calculated from the difference in oxygen content of blood entering and leaving the oxygenator and from the screen flow; it included both chemically combined and dissolved oxygen. The pH was determined at 37° C. in a Cambridge Research Model pH meter. The carbon dioxide pressure (pCO_2) was estimated from the Singer-Hastings nomogram.[5] Methods used for the in vitro study were different only in that the percentage saturation of hemoglobin was determined with a Wood cuvette oximeter,[6] and the calculated rates of oxygen transfer did not include any oxygen in physical solution.

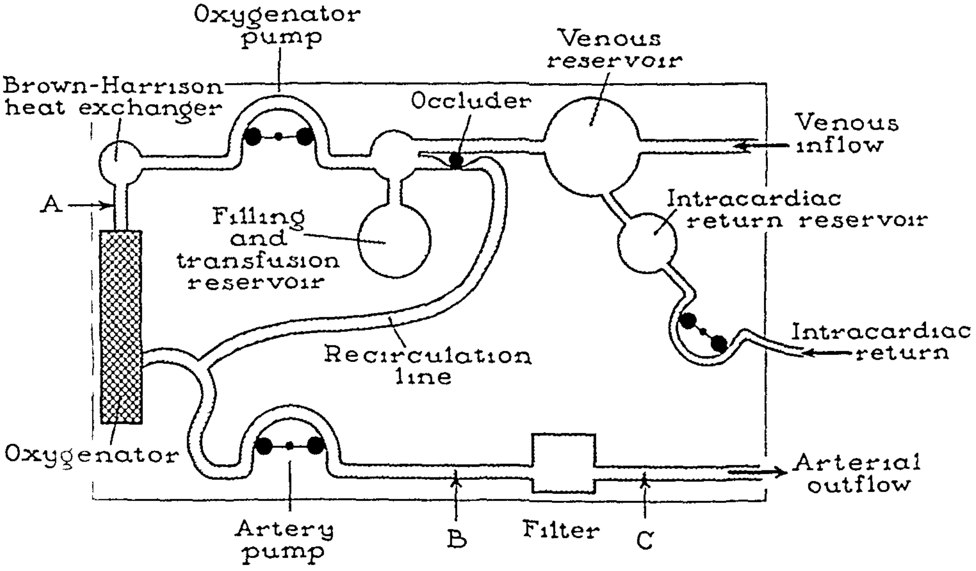

Fig. 1.—Flow circuit of Mayo-Gibbon pump oxygenator.

The surface area in square meters for patients weighing more than 15.5 kilograms was obtained from a height-weight nomogram based on the DuBois formula. The surface area of patients weighing 15.5 kilograms or less was obtained from a table based on weight.[7] Basal consumption of oxygen in the first group was calculated from values based on age, sex, and surface area[8]; in the second group, it was determined from values based on sex and weight.[9]

PROCEDURE

The performance of the oxygenator was studied during the normothermic perfusion of 17 patients and during one in vitro study. During total cardiopulmonary bypass, the recirculation line was closed (see Fig. 1 for the flow circuit). Blood passed from the venous reservoir through the oxygenator once and then into the arterial system of the patient. The oxygenator was ventilated with 98 per cent oxygen and 2 per cent carbon dioxide at a flow rate of 10 L. per minute. The design of the individual screen (30 cm. wide, 60 cm. high) has been published.[1] Screen flows were established prior to the institution of perfusion and remained unchanged throughout each individual perfusion. Anesthesia was accomplished by the use of thiopental sodium, nitrous oxide, and succinylcholine.

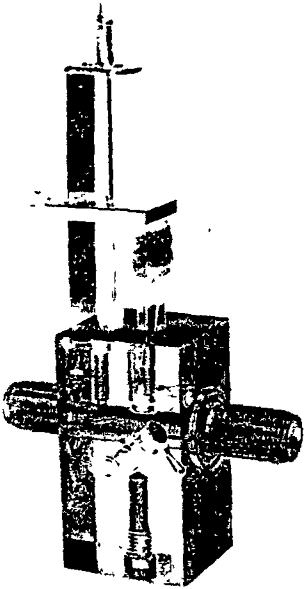

Fig. 2.—Manifold with thermistor probe, oxygen electrode, and sample cock.

Fig. 2 illustrates the manifold that provided for the placement of an oxygen electrode, a thermistor and a sample cock in the lines entering the oxygenator (*A* in Fig. 1) and leaving it (*B* in Fig. 1). In a preliminary study, the oxygen tensions observed at site *B* were not different from those observed at a second site distal to the arterial filter (*C* in Fig. 1). In Cases 1 through 10, oxygen tensions were determined at sites *A* and *B* at 1-minute

Table I. Data During 17 Clinical Perfusions With the Vertical-Screen Oxygenator

			PERFUSION FACTORS			BLOOD ENTERING OXYGENATOR*			BLOOD LEAVING OXYGENATOR					
CASE	SURFACE AREA (SQ. METERS)	BASAL OXYGEN UPTAKE (PREDICTED) (ML./MIN./SQ. METER)	SCREENS (NUMBER)	SCREEN FLOW (ML./MIN.)	HEMOGLOBIN (GM./100 ML.)	pO_2† (MM. HG)	OXYGEN CONTENT (VOL. %)	HEMOGLOBIN SATURATION (%)	pO_2† (MM. HG)	OXYGEN CONTENT (VOL. %)	HEMOGLOBIN SATURATION (%)	pH	pCO_2 (MM. HG)	OXYGEN ADDED (ML./MIN./SCREEN)
1	1.48	—	13	228	—	37	—	—	110	—	—	—	—	—
2	0.60	—	7	209	—	60	—	—	205	—	—	—	—	—
3	1.15	—	13	212	—	50	—	—	280	—	—	—	—	—
4	0.80	—	9	204	—	43	—	—	180	—	—	—	—	—
5	0.74	—	8	222	—	45	—	—	105	—	—	—	—	—
6	1.42	142	12	237	12.5‡	40	12.7	75	165	17.7	100	7.42	25	11.7
7	0.92	178	10	219	12.4‡	43	10.2‡	61	190	17.7‡	100	—	—	16.4
8	1.20	163	13	222	13.2	45	14.2	79	235	18.7	100	7.43	25	10.1
9	1.25	146	13	222	12.2‡	40	10.9‡	66	135	17.2‡	100	7.36	30	13.9
10	1.21	158	13	223	12.0	39	11.4	70	230	16.4‡	98	7.44	21	11.2
11	0.56	163	6	224	14.0	—	13.0	69	—	18.6	98	—	—	12.5
12	0.85	183	7	291	15.5	—	14.6	70	—	19.8	94	—	—	15.1
13	1.01	166	9	274	12.9	—	11.7	67	—	17.3	99	—	—	15.4
14	1.81	161	14	279	13.3	—	11.4	64	—	17.0	94	—	—	15.7
15	1.19	173	10	286	12.7	—	11.2	65	—	17.3	99	—	—	17.4
16	0.35	143	3	280	13.9	—	11.8	63	—	17.1	90	—	—	14.8
17	0.69	157	6	277	13.0	—	11.2	64	—	16.8	95	—	—	15.4

*Not synonymous with mixed venous blood (see flow circuit, Fig. 1). Includes all intracardiac return aspirated from the heart and returned to the machine.

†Values of pO_2 are those most representative of all values observed during perfusion (Cases 1-5) or those observed at time of withdrawal of samples (Cases 6-10).

‡Only single values for oxygen capacity and oxygen content were available in these cases; mean values based on two determinations were used in all the other cases.

intervals. In Cases 6 through 17, duplicate samples of blood were drawn at these sites 15 to 20 minutes after institution of perfusion and were analyzed for oxygen content, oxygen capacity, carbon dioxide content, and pH.

In the in vitro study, dog blood at 37° C. was desaturated in an isolated dog-lung preparation and pumped to an experimental oxygenator containing a single screen (25 cm. wide, 60 cm. high). A range of flow rates* (58 to 465 ml. per minute) or saturation (1 to 69 per cent) or both for the blood entering the oxygenator was obtained by altering the pump setting or by changing the gas mixture with which the isolated dog lung was being ventilated.

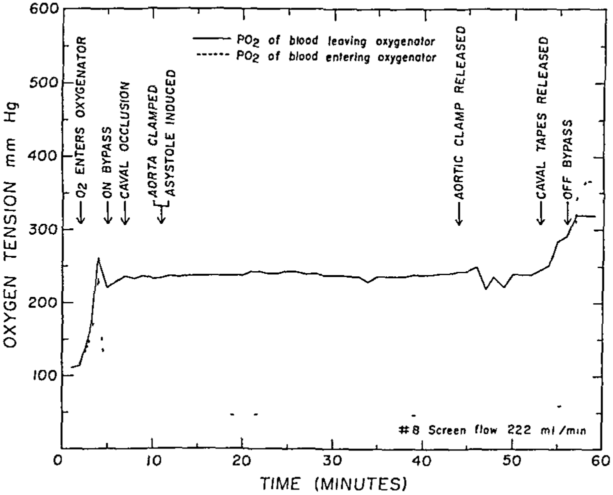

Fig 3.—Oxygen tension in blood entering and leaving the oxygenator during whole-body perfusion in Case 8 See text for details

RESULTS

The accompanying Table I summarizes all data obtained during the clinical perfusions In Cases 1 through 11, the screen flow ranged from 204 to 237 ml. per minute per screen, averaging 220; in Cases 12 through 17, the screen flow ranged from 274 to 291 ml. per minute per screen, averaging 280. The hemoglobin content ranged from 12.0 to 12.5 Gm. per 100 ml. of blood, averaging 13.1. The remaining data in the Table will be considered in conjunction with Figs 3 through 6

The pattern of changes in oxygen tension observed in Case 8 (Fig. 3) was present in the 10 perfusions in which oxygen tension was measured. After filming, equilibrium was reached between the oxygen in the blood and that in the air within the oxygenator. With the introduction of 98 per cent oxygen, the oxygen tension in the blood leaving the oxygenator began to increase. With the entry of desaturated blood from the patient, the oxygen tension in the blood entering the oxygenator decreased precipitously for 1 to 2 minutes and then became constant. During the 35 minutes of total bypass, the tension of oxygen in the blood entering and leaving the oxygenator was essentially constant. Release of the tapes on the venae cavae resulted in a reduction of the venous return to the machine. As a consequence, recirculation of blood through the oxygenator occurred, with an increase in the tension of oxygen in the blood entering and leaving the oxygenator. While a range of oxygen tension was observed in blood entering (37 to 60 mm. Hg) and leaving (105 to 280 mm. Hg) the oxygenator in the 10 cases, the tension of oxygen in blood entering and leaving the oxygenator was always steady in each individual perfusion during the period of total bypass.

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*Flow rates in this study were the observed rates multiplied by $\frac{30}{25}$ in order to be comparable to the rates of the clinical perfusion, in which a screen 30 cm in width was used

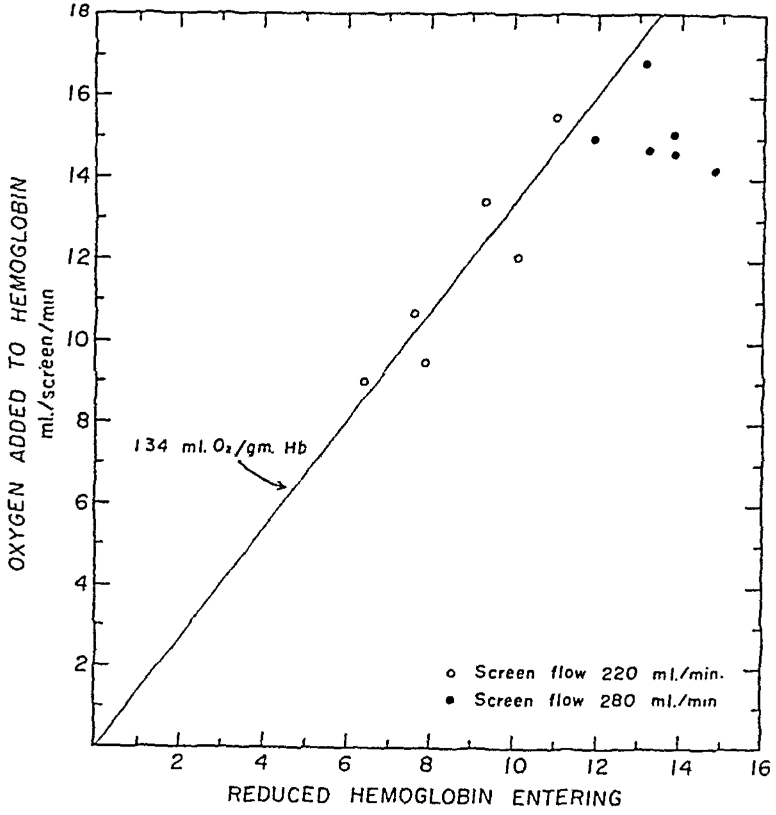

Fig. 4.—Performance of oxygenator screen at flows of 220 and 280 ml. per minute per screen. See text for details.

Fig. 4 presents the performance of the stationary vertical-screen oxygenator. The straight line indicates complete conversion of reduced hemoglobin to oxyhemoglobin. Points lying on this line indicate 100 per cent saturation of the blood leaving the oxygenator and were observed at screen flows of 220 ml. per minute; points below the line indicate desaturated blood leaving the oxygenator and were uniformly observed at screen flows of 280 ml. per minute.

At the former flow the rate of oxygen transfer was directly related to the rate at which reduced hemoglobin entered the oxygenator, at the latter flow, while both these rates were generally greater, the relationship between the two rates is not clear and is clarified in the in vitro study (Fig 5) The amount of reduced hemoglobin entering the oxygenator was increased by keeping the actual rate of flow constant and increasing the degree of desaturation in the incoming blood and also by increasing the rate of flow while maintaining a fairly constant incoming saturation Increasing the rate at which reduced hemoglobin entered the oxygenator by either maneuver resulted in an increase in the rate of oxygen transfer in the oxygenator

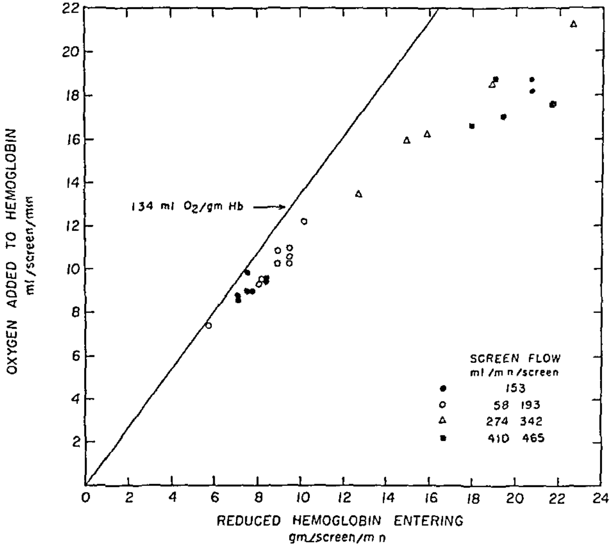

Fig 5—In vitro performance of the stationary vertical screen oxygenator using dog blood with an oxygen capacity of 18 9 volumes per cent

Fig 6 indicates the relationships in 12 patients between the observed rate of oxygen transfer in the oxygenator and the surface area of the patient The mean of all observations was 131 ± 20 (S D) ml of oxygen per minute per square meter of surface area, deviations from the mean amounting to 32, 47, and 22 ml of oxygen in Cases 6, 7, and 8 were the major contributions to the magnitude of the standard deviation and are believed to be partly the result of sampling and analytic errors The mean value of the basal oxygen uptake predicted for these 12 patients was 161 ml per minute per square meter The observed oxygen transfer was in one instance equal to and in 11 instances smaller than the predicted basal oxygen uptake air within the oxygenator. With the introduction of 98 per cent oxygen, the oxygen tension in the blood leaving the oxygenator began to increase. With the entry of desaturated blood from the patient, the oxygen tension in the blood entering the oxygenator decreased precipitously for 1 to 2 minutes and then became constant. During the 35 minutes of total bypass, the tension of oxygen in the blood entering and leaving the oxygenator was essentially constant. Release of the tapes on the venae cavae resulted in a reduction of the venous return to the machine. As a consequence, recirculation of blood through the oxygenator occurred, with an increase in the tension of oxygen in the blood entering and leaving the oxygenator. While a range of oxygen tension was observed in blood entering (37 to 60 mm. Hg) and leaving (105 to 280 mm. Hg) the oxygenator in the 10 cases, the tension of oxygen in blood entering and leaving the oxygenator was always steady in each individual perfusion during the period of total bypass.

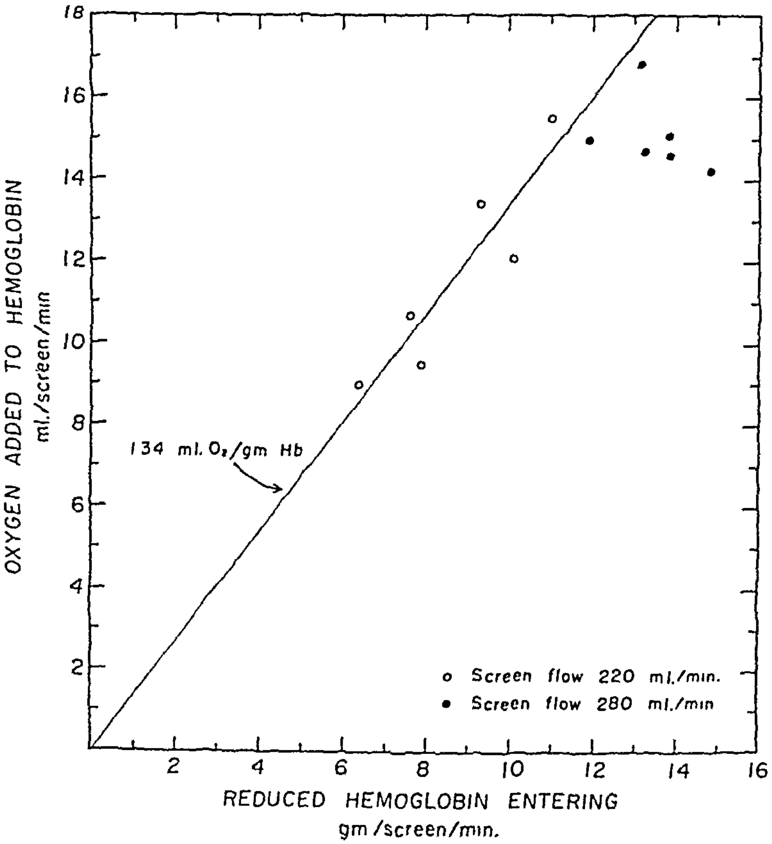

Fig. 4.—Performance of oxygenator screen at flows of 220 and 280 ml. per minute per screen. See text for details.

Fig. 4 presents the performance of the stationary vertical-screen oxygenator. The straight line indicates complete conversion of reduced hemoglobin to oxyhemoglobin. Points lying on this line indicate 100 per cent saturation of the blood leaving the oxygenator and were observed at screen flows of 220 ml. per minute; points below the line indicate desaturated blood leaving the oxygenator and were uniformly observed at screen flows of 280 ml. per minute.

further, that the oxygen uptake by the patient was steady. At flow rates of 280 ml. per minute, single observations were made 20 minutes after the establishment of the perfusion. It is believed that these measurements are also representative of the steady state for several reasons. First, in the aforementioned study, oxygen tensions became steady well before 20 minutes. The second reason is evident from the oxygen-transfer rates (ml./min./sq. meter), in which no difference is apparent in the rates calculated during periods of constant tension at flows of 220 ml. per minute per screen and in those calculated from single observations made 20 minutes after the establishment of perfusion at flows of 280 ml. per minute per screen. These observations further imply that the steady state at screen flows of the latter rate was arrived at without a change in the oxygen uptake by the patient. It will be remembered that these patients were perfused with incompletely saturated blood.

The performance characteristics of the oxygenator explain these observations. The rate of oxygen transfer in the oxygenator is related to the rate at which reduced hemoglobin enters the oxygenator. This relationship is such that, up to a certain rate of incoming reduced hemoglobin, the rate of oxygen transfer will be sufficient to saturate fully all reduced hemoglobin with oxygen. When the presentation of reduced hemoglobin exceeds this rate, the rate of oxygen transfer, while greater than that in the previous situation, will not be sufficient to saturate fully all entering reduced hemoglobin. Desaturated blood then will leave the oxygenator. The greater the degree by which this certain rate is exceeded, the greater is the degree of desaturation in blood leaving the oxygenator, but also the greater is the rate of oxygen transfer in the oxygenator. Therefore, a necessary consequence of operating the oxygenator in such a fashion that desaturated blood leaves it is that the arteriovenous difference across the oxygenator and, therefore, across the patient is widened, and actual levels of oxygen in the patient are lower.

SUMMARY

During normothermic perfusions at a blood flow of 220 ml. per minute per screen, the vertical-screen oxygenator, ventilated with 98 per cent oxygen and 2 per cent carbon dioxide, provided arterial blood with oxygen tensions of 105 to 280 mm. Hg and oxygen saturations of 98 to 100 per cent that remained constant throughout the perfusions. Increasing the screen flow to 280 ml. per minute per screen resulted in blood that had venous oxygen saturations of 63 to 70 per cent leaving the oxygenator with oxygen saturations of 90 to 99 per cent. The oxygen transferred by the oxygenator and utilized by the patients ranged from 99 to 178 ml. per minute per square meter of body surface. The characteristics of the oxygenator permit the attainment of a steady state by increasing its rate of oxygen transfer when presented with increased amounts of reduced hemoglobin per minute.

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A ROTATING DISC BLOOD OXYGENATOR AND INTEGRAL HEAT EXCHANGER OF IMPROVED INHERENT EFFICIENCY

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THE ROTATING DISC, filming blood oxygenator has proved to be a very satisfactory instrument In its most popular form (the variation by Kay and Cross[1]), it combines inherent simplicity with minimal trauma to the blood Yet, satisfactory as they are, current forms of the disc oxygenator could be improved in two important respects (1) it is desirable for the oxygenator to contain less blood while exposing a larger surface to oxygen, and (2) a larger heat transfer surface is desirable for rapid cooling and warming of the contained circulating blood

The currently popular type of 12 cm diameter disc oxygenator is limited in its oxygenating efficiency largely by the occurrence of foaming if the discs are rotated too rapidly It is restricted to a rather large contained volume of blood (in relation to the disc area exposed), mainly for the same reason, because foaming tends to occur if the level drops too low at normal rotational speeds, so that a rather large area of disc must be under blood at all times This is most likely because at any point on the lower periphery of the disc where it is not immersed in blood, gravity is added to the centrifugal force and so tends to cause splashing when the blood level is low Finally, the oxygenator is limited in its ability to transfer heat by the rather small area of blood in direct contact with the casing which can be warmed or cooled

It is obvious that the oxygenating efficiency of a disc oxygenator is related to the area of disc submerged in the blood trough compared with the wetted area of the disc exposed to oxygen Therefore, a disc oxygenator is most efficient (as measured by ratio of oxygenating surface to contained volume) if the disc is very large and dips only slightly into the blood trough (Fig 3) However, the practical size of the disc is limited by the limit on the linear speed of the disc rim due to foam formation at high speeds

Experimentally, it can be shown that when discs rotate while dipping into blood a higher rim speed can be achieved without foam formation if the clearance

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between disc edges and casing is very small, so that a continuous meniscus of blood is continually present between disc and casing all around its periphery. If such a meniscus of blood is maintained all around the disc, then obviously the whole adjacent interior cylindrical surface is wet with non-stagnant blood and thus can be used as a heat-transfer surface.

Based on these principles, an oxygenator has been designed which incorporates marked improvements in oxygenating efficiency and heat-transfer characteristics over current disc oxygenators.

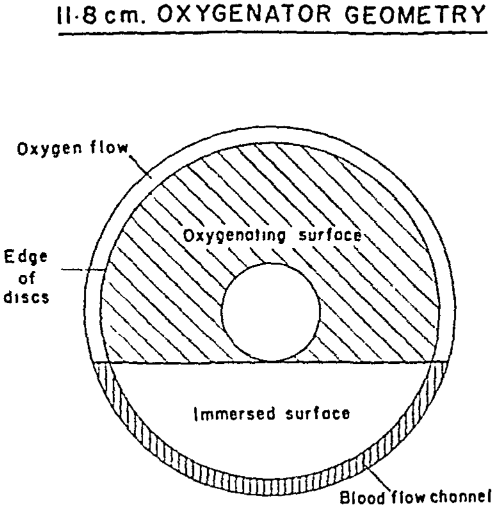


Fig. 1.—Diagram of the geometry of an 11.8 cm. disc oxygenator.

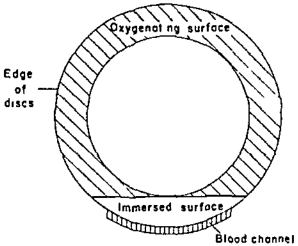
DESIGN DESIDERATA

Disc oxygenators of 11 to 12 cm. disc diameter are presently widely used, and unless significant improvements on their performance could be realized the development of a new one would be unwarranted. Consequently, emphasis is laid in this report on direct comparisons with a standard 11.8 cm. disc oxygenator.[1]

Geometry of the 11.8 Cm. Oxygenator.—A 21 inch long oxygenator with one hundred 11.8 cm. discs has a priming volume of 2.5 liters and, thus primed, an oxygenating surface of 1.33 square meters (per revolution), which is the maximum obtainable. In use, the discs are usually immersed to 4.1 cm., which is 69.2 per cent of their radius. There is an 0.56 cm. clearance between the periphery of the disc and the cylinder or casing, through which blood and oxygen can flow. The recommended maximum rotation speed is usually 120 r.p.m. The geometry is shown, full size, in Fig. 1.

Geometry of Our New Oxygenator.—In order to improve the ratio of oxygenating surface to priming volume it is clear, as already mentioned, that the discs must be immersed to a much smaller fraction of their radius, so that only a narrow annulus becomes wetted. This is illustrated in principle in Fig. 2 (assuming the same diameter discs were used).

Since the immersed surface (plus the cross-sectional area of the blood flow channel) is proportional to the priming volume, it is obvious by visual comparison between Figs. 1 and 2 that the *ratio* of oxygenating surface to priming volume is much better in Fig 2 than in Fig 1, they are, respectively, 1 15 and 0 58* However, the oxygenating surface is considerably smaller than in Fig 1, 0 88 square meters as against 1 33 square meters Therefore, to obtain adequate oxygenation with this more efficient geometry we must increase the diameter of the discs A diameter of 8¼ inches (21 cm) is a convenient compromise However, whereas centrifugal force acting on blood at the periphery of an 11 87 cm disc rotating at 120 r p m is 0 96 g , on a 21 cm disc it is



21cm OXYGENATOR GEOMETRY

Fig 2 —Diagram of the geometry of our new 21 cm disc oxygenator

1 7 g The tendency for droplets to be flung off the discs and splash against the cylinder wall is therefore nearly doubled with the larger disc, with consequent danger of foam formation We have reduced this danger by reducing the clearance between the discs and the cylinder wall to 0 016 inches, which is small enough to be easily and consistently spanned by the centrifugally formed blood meniscus The blood then touches both disc and casing all the way around, and foam formation is much reduced

Since this arrangement leaves room for neither blood nor oxygen to flow axially through the oxygenator, other provisions must be made We have provided blood flow by a longitudinal channel at the bottom of the cylinder, the cross section of which is a concentric annular segment 0 63 cm deep, subtending an angle of about 64 degrees This channel has a cross sectional area equivalent to a 1 22 inch diameter circle, and will permit a 4 liter per minute gravity flow under a head of 2 inches† (This, therefore, will be the order of maximum difference in level between the entry and discharge ends of the unit)

Oxygen flow is made possible by one ⅝ inch diameter hole in each disc near the shaft On assembly each hole is oriented at 180 degrees to those in adjacent discs, so as to encourage mild oxygen turbulence between them

Other important considerations in design are applicability of cleaning techniques, and ease in sterilization The present apparatus has therefore been designed and built entirely of parts which can be autoclaved, and access for cleaning is provided to every place touching blood Cracks and recesses hard to find with a brush have been avoided

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*The units used are square meters per revolution (100 discs) divided by liters This ratio may be regarded as a measure of efficiency

†Obtained by actual test

Detailed Design Specifications.—

1. The main cylinder and discs are made of stainless steel.
2. The end-covers are made of transparent Kel-F-plastic, reinforced with aluminum, which latter does not come in contact with the blood.
3. The blood inlet and outlet are vertical, below the discs.
4. The blood outlet is provided with an anti-vortex baffle.
5. A jacket is provided for hot or cold water circulation to provide temperature control.
6. A two-stage rubber belt speed-reducing drive with motor attached to the unit are provided, so that the unit can be freely suspended and continuously weighed for accurate volume control. A voltage generator is similarly attached for speed measurements.
7. Electric light bulbs are mounted inside end-covers to facilitate observation of blood levels.
8. A clip is provided at the output end of the oxygenator for a photocell level-sensing device.

CLEANING AND MAINTENANCE

The procedures for cleaning and maintenance of an oxygenator are of crucial importance. Our entire unit can be disassembled after use, and each part individually scrubbed and treated. The nearer the entire unit can be made chemically clean the better. As a minimum, every part which can possibly touch blood should be scrubbed individually with appropriate detergent, then rinsed long and hard. All parts should then be dried and coated with baked silicone before each use. Several commercial silicone preparations are satisfactory, we have used an acetone solution of Dow-Corning DC1107. All parts are dipped in this solution, and then baked at approximately 100° C. for one hour.

Ideally, the previous silicone coating should be removed after each use, and all organic matter should be taken off by strong acid or a strong oxidizing agent. Where cleaning and maintenance are to be done in the hospital, complete disassembly with attention to each part may be necessary. However, where it is possible to handle washing in bulk, and where strongly caustic solutions can be handled safely in larger tanks, the whole assembly of discs-on-shaft can be handled as a single unit without taking it apart.

By an arrangement with a local commercial laboratory, we have found it convenient to have the detailed cleaning take place outside the hospital. We will describe our technique as it has been found quite satisfactory, but a similar routine could easily be set up in many large hospitals, or modified by individual circumstances. Our procedures as described were planned with a view to: (a) transfer of a high proportion of the cleaning labor load from the hospital staff to an outside commercial laboratory; (b) reduction of total man-hours of cleaning per perfusion; (c) destruction of all pyrogenic substances; and (d) removal after each perfusion of the silicone coatings (which otherwise accumulate) and recoating with a fresh surface. We have accomplished these aims in the following manner.

For an average of five perfusions per week, we have available two cylindrical stainless steel oxygenator casings and eleven disc shaft assemblies The disc shaft assemblies are processed in rotation outside the hospital * The discs are never disassembled from the shafts and handled singly, but each shaft disc assembly is processed as a unit Immediately after each perfusion the oxygenator is rinsed out with water and detergent, and the shaft disc assembly is then removed from the casing To facilitate transport it is mounted in a light stainless steel cradle which forms the lid of a light galvanized steel box for protection in (truck) transport After insertion in this box the assembly is autoclaved (for the protection of the processors) and shipped to the processor Processing is done there by immersion in appropriate liquids without removal from the cradles

The treatment consists of

1 Immersion in 5 per cent potassium hydroxide in alcohol at 60 to 70° C This removes the silicone coating
2 Rinsing in water
3 Immersion in concentrated (commercial) nitric acid This cleans the discs, oxidizes all organic materials and so destroys pyrogens
4 Rinsing in distilled water
5 Drying
6 Silicone coating by immersion in standard acetone solution of silicone DC1107
7 Drying and baking
8 Final spraying with distilled water (pyrogen free)
9 Re insertion in box and shipment to hospital

The treatment of the casing consists at present of a scrubbing with water and detergent followed, after rinsing by flooding with a strong (0 5 per cent) solution of potassium permanganate For the sake of consistency it is intended to substitute treatment with nitric acid No silicone coating is applied to the casing, since its surface constitutes only a small fraction of the total wetted surface Stainless steel endplates are provided with trunnions, permitting the casing to be one third filled with nitric acid, and swung so that the entire surface is treated After a final rinsing with distilled water the casing is ready to receive a shaft disc assembly from the revolving stock kept in reserve at the hospital

When fully assembled, the oxygenator is autoclaved not more than 24 hours before perfusion No antifoam is used The approximate disposition at any one time of the eleven shaft disc assemblies is as follows in transit, 4, in process, 4, in use, 1, in reserve, 2, which makes a total of 11

This type of rotation of several internal assemblies is efficient when a large number of perfusions are performed, and cleaning is to be done by "mass production" However, it is reasonably easy to carry out one perfusion daily

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*Cutter Laboratories Berkeley California using one casing and two disc-shaft assemblies. In this case, cleaning must be done inside the hospital by a technician assigned especially to this job. One disc-shaft assembly is cleaned while the other is being used. The casing (which is quickly cleaned) is finished immediately after the perfusion of the day. Then the clean disc-shaft assembly is slid into it, and the whole unit is sent to the autoclave to be sterilized for the next morning's run.

PERFORMANCE

A. *Theoretical.*—Fig. 3 shows the variation of priming volume and oxygenating surface with blood level (above the lower horizontal tangent to the discs) for both an 11.8 cm. diameter 100 disc oxygenator and our 21 cm. 96 disc unit.

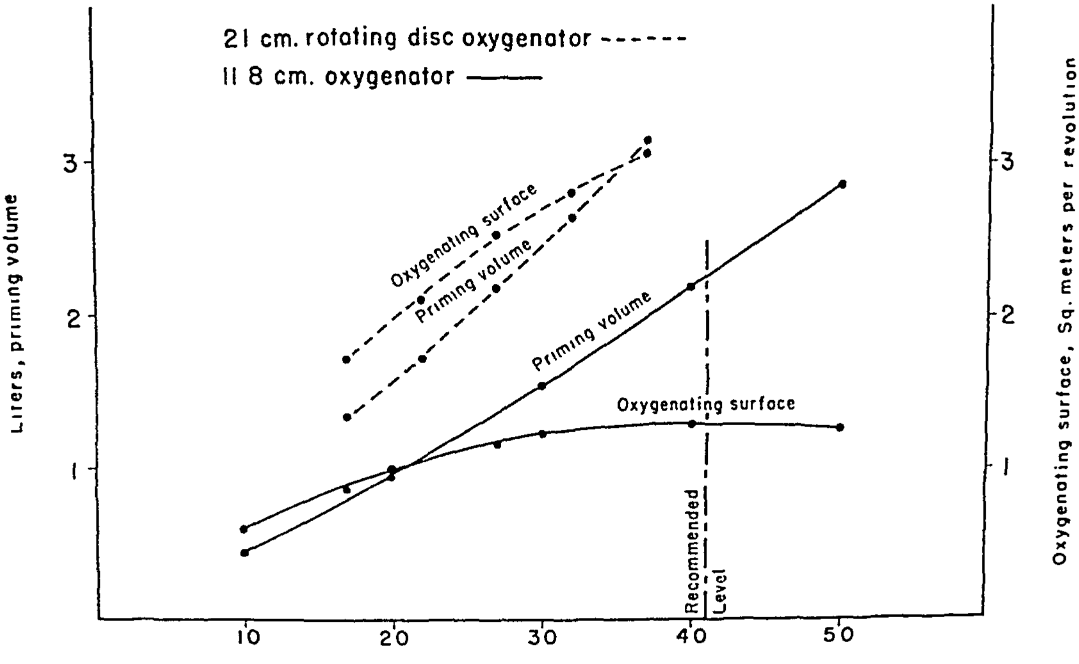

Fig. 3.—Diagram comparing oxygenating surface and priming volume at varying blood levels in both the 11.8 cm. and 21 cm. disc oxygenators.

The values are obtained by geometric computation—the priming volume graphs therefore do not take account of the volume of blood adhering to the discs above blood level; tests have shown the correction to be of the order of 10 per cent. It will be noted that the maximum oxygenating surface (per revolution) of the 11.8 cm. diameter unit is 1.33 square meters, compared with 2.55 square meters for our 21 cm. diameter unit at the same priming volume (2.25 liters). The latter figure is not a maximum. If a priming volume of 3 liters (plus correction for wetted oxygenating surfaces) is accepted, the oxygenating surface will be 3.0 square meters per revolution, or 2.25 times the maximum obtainable with the 11.8 cm. diameter disc machine.[*]

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[*] In our 21 cm. unit there is an additional 0.3 square meters of static oxygenating surface provided by the (continuously wetted) cylinder wall. Since, however, the rate at which this blood film is renewed cannot be calculated, this surface has been ignored.

The variation of oxygenating surface with priming volume is shown in Fig. 4 for both oxygenators. (Note: the ordinate units in this graph are square meters per minute at 120 r.p.m.) Fig. 5 shows the variation of "efficiency," i. e., ratio of oxygenating surface in square meters per revolution to priming volume in liters against oxygenating surface.

B. *Practical.*—The oxygenator just described* has been used for perfusion of 22 patients with congenital and acquired heart disease at the San Francisco-Stanford Hospital. Several patients were perfused for periods of over one hour. Two severely ill patients (with tetralogy of Fallot) were on total perfusion for 80 minutes and 100 minutes, respectively, and both convalesced rapidly, with almost no postoperative fever or other difficulty. Hemolysis under operating room conditions has been unmeasurable, because the major cause of hemolysis is the suction of blood from the open heart by the "coronary sucker," and hemolysis caused by the oxygenator has been too small in comparison to measure separately. In one 25-minute period of full perfusion in an adult, during which the coronary return suction system was not used, the plasma

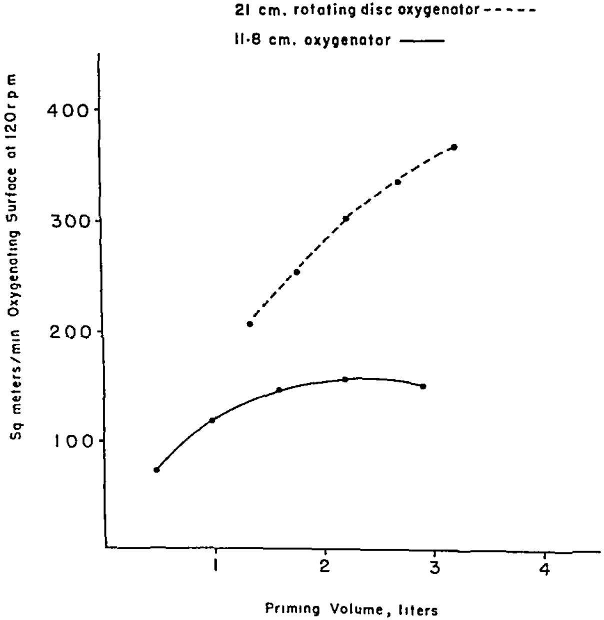

Fig 4 —Diagram comparing oxygenating surface at varying priming volumes in both the 11.8 cm and 21 cm disc oxygenators

hemoglobin at the end of the 25-minute period was less than at the beginning of the period. The largest patient perfused weighed 170 pounds. There has never been difficulty in maintaining arterial saturation over 90 per cent.

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*Manufactured by Hallikainen Instruments, Berkeley, California.

The apparatus, including all tubing, filter, etc., is easily primed for an adult with six units (3,000 c.c.) of heparinized blood, much less if a small child is the patient.

It is our clinical impression that the series of patients perfused with this oxygenator have been less sick in the postoperative period than patients perfused with previous machines. It is impossible to make exact comparisons, but certainly fever used to be common in the first postoperative days, and has become very much less common, and, when present, is less severe. We have the clinical impression that pulmonary symptoms are also less, and that the postoperative roentgenograms are clearer.

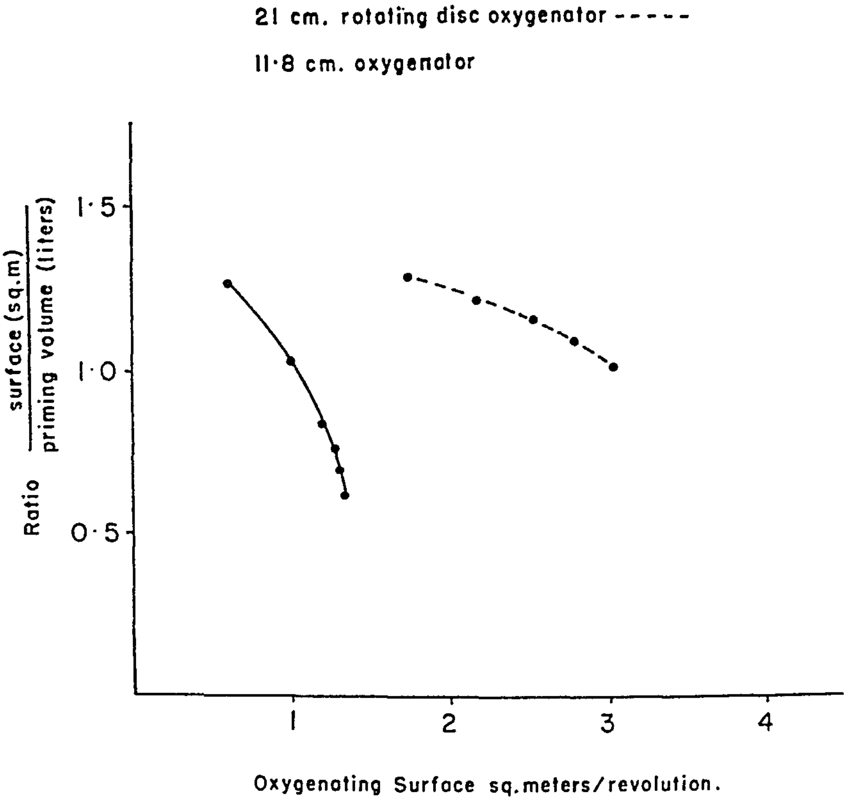

Fig. 5.—Diagram showing surface to priming volume ratio against varying oxygenating surfaces in both the 11.8 cm. and 21 cm. disc oxygenators.

Foaming in the oxygenator has never occurred, though no antifoam has been used. There has been no severe postoperative bleeding, and the bleeding in general has been as little as or less than that when previous machines were used.

All patients have had their body temperatures electively lowered to 32° C. at least, many to much lower temperatures. The data on type of induced hypothermia are extensive and must form the subject of a separate communication, but it is appropriate here to stress the ease with which hypothermia may be

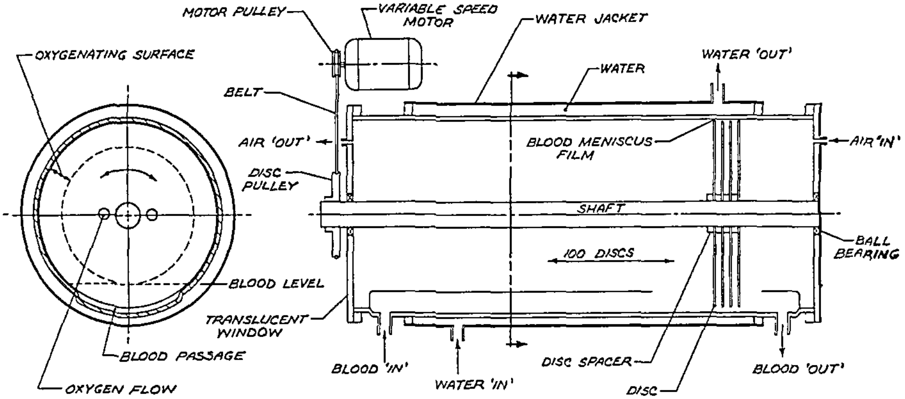

Fig 6 —Sectional diagrammatic sketch of 21 cm disc oxygenator

induced, and then the patient rewarmed, without the use of a separate blood heat-exchanger. Body temperatures (in adults) have been routinely lowered at the rate of roughly 0.67° C. per minute, and raised at the rate of roughly 0.5° C. per minute. This represents heat transfer at a rate of over 50 kilogram-calories per minute. Much faster cooling and rewarming rates are possible in children.

PUMP AND CONTROL APPARATUS

The foregoing description has applied to the oxygenator alone. Obviously an oxygenator needs a pumping and control system, but this oxygenator could be adapted to many existing pumping systems. In our own use we have incorporated it in a chassis which we will describe.

The oxygenator (with its water-jacket, disc rotation drive, light source, and generator-tachometer) is suspended from two steel bending beams which are adapted with Baldwin-Lima-Hamilton SR4 strain gauges to sense weight. Weight of the unit (with its contained blood) is read out on a visible indicator (Minneapolis Honeywell) and also fed to a control system linked to the drive of the arterial pump. The unit can then be adjusted to sense the volume of blood in the oxygenator within 10 or 20 c.c. of blood, and to adjust automatically the speed of the delivery pump (the arterial pump) to maintain a constant volume of blood in the artificial lung. This automatic control can be bypassed with a manual control as desired, but it makes it possible for the operator to maintain very strict sensing of the total blood volume of the patient, and also greatly reduces the danger of air embolism to the patient (from the blood level in the oxygenator accidentally dropping too low). We have used Gibbon-type De Bakey pumps for both the arterial delivery and intracardiac suction, and we incorporate a filter and air-trap in the delivery system.

To reduce as much as possible the chance for human error we have incorporated also several safeguards, many of which we had found useful with previous oxygenators.[2] These include:

1. An audible signal (fed by photocell) if the blood level in the oxygenator drops below a set level.
2. Automatic arrest of the arterial pump if the blood weight drops below a preset amount.
3. An electrically lighted plastic window for observing blood level.
4. An automatic audible warning if the line pressure in the arterial delivery line rises above 300 mm. Hg, with automatic cut-out of arterial pump.
5. A manometer indicating delivery-line pressure.
6. A tachometer showing speed of oxygenating disc shaft.
7. An alternate electrical control system (direct current) for use in case of alternating current line failure.
8. Provision for manual pumping (with detachable handle) in case of mechanical or other failure.
9. Two electric thermometers for blood and water-jacket temperature.

SUMMARY

A new disc-type blood oxygenator has been described which exposes a larger area of oxygenating surface compared with the volume of contained blood than previous disc oxygenators.

Through its inherent design, the oxygenator functions also as a highly efficient heat exchanger.

Details of design, performance, and maintenance are presented.

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A MODIFICATION OF THE CLOWES MEMBRANE LUNG

E. Converse Peirce, II, M.D., Knoxville, Tenn.

No clinical substitute for the normal lung is ideal. In the laboratory, the homologous lung approaches perfection, but unfortunately it cannot be used clinically. Heterologous lungs and all presently available machines are imperfect for one or more reasons: they are emboli-prone, trauma is too great, there is an element of unreliability, priming volume is excessive, they are too complicated, they are too expensive, or they are simply too tiresome to assemble, sterilize, or operate. Probably no real solutions to the problems are possible where gas and liquid phases are not clearly separated, as by a membrane. With the membrane lung, practically all of the present defects can be obviated to some degree when very large flows are not required. Some difficulties, such as complicated monitoring, can be eliminated entirely. We believe it is important to present our modification of the Clowes membrane lung[1, 2] since it can be readily constructed and used by any interested research worker or clinician. With more general experience will come an appreciation of its advantages. Attention to the advantages of the membrane lung should permit production of a satisfactory disposable unit.

A mechanical lung substitute should be called an artificial lung and not an oxygenator, since it must provide adequate carbon dioxide elimination as well as oxygenation (Table I). For every 5 c.c. of oxygen taken up by the blood, 4 c.c. of carbon dioxide must be removed. Failure to maintain a proper balance leads to an unphysiologic pH and may be quite dangerous. The functional unit of the human lung is the alveolus and there is considerable intellectual appeal and practical advantage to the construction of an artificial lung which comprises the elements of air sac, membrane, and capillaries. It is important to realize that one is endeavoring to substitute only for the basal functions of the normal lung and that for only a limited time. These basic concepts set the stage for the development of a membrane lung.

The necessary physical condition for a balanced function of the artificial lung are a pO_2 above 80, a pCO_2 below 50, and a pH of about 7.3 to 7.4. In order to understand the requirements for such a lung, the behavior of oxygen and carbon dioxide in blood and in relation to the best available membranes

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TABLE I HUMAN LUNG

Functions		*Unit*
Oxygenate blood	Alveolus	Air sac
Eliminate carbon dioxide		Membrane
Maintain pH		Capillaries
	Range	
Ventilation		5 to 100 L/min
Blood flow		3 to 30 L/min
Gas exchange		*200 to 2,400 c c/min*

must be known In solution, these two gases behave quite differently Oxygen is relatively insoluble, practically all being carried in chemical combination with hemoglobin Since the diffusion of a gas through a liquid is directly proportional to its solubility, oxygen diffuses very slowly and a thin film is necessary for adequate oxygen exchange Carbon dioxide is comparatively very soluble and diffuses about 30 times as fast as oxygen, so that the thickness of the blood film has relatively less bearing on carbon dioxide exchange Now, the best available membrane for oxygen and carbon dioxide transfer is Teflon Because of strength limitations, the thinnest useful membrane is $\frac{1}{2000}$ of an inch The transmission of oxygen through such a membrane has been measured with the platinum polarograph[3] and the results confirmed using a diffusion chamber[5] The relative diffusibility of oxygen and carbon dioxide are illustrated in Table II Although carbon dioxide diffuses much more readily than oxygen, the physiologically tolerable pCO_2 results in a relatively unfavorable diffusion rate The conclusions resulting from study of the best available membrane and the relative behavior of oxygen and carbon dioxide in blood follow

TABLE II TRANSMISSION OF OXYGEN AND CARBON DIOXIDE THROUGH 0 0005 IN TEFLON MEMBRANE AT BODY TEMPERATURE IN C C/M²/MIN

	AS GAS AT ONE ATMOSPHERE PRESSURE	THEORETICAL IN MEMBRANE LUNG*	ACTUAL IN MEMBRANE LUNG	PER CENT EFFICIENCY OF LUNG
Oxygen	45	40	10	25
Carbon dioxide	120	8	8	100

*PO_2 690 mm Hg pCO 50 mm Hg

TEFLON MEMBRANE LUNG

A Carbon dioxide is very soluble and diffuses rapidly, therefore (1) the membrane and permissible pCO_2 determine CO_2 elimination, (2) because pCO_2 must be low, CO_2 elimination is limiting factor in lung function, and (3) it dictates the necessary membrane area

B Oxygen is one thirtieth as soluble and diffuses slowly, so that (4) oxygenation depends on blood film thickness and transit time and hence on lung design, (5) it is relatively independent of the membrane using reasonable film thicknesses, and (6) with adequate CO_2 elimination, there is considerable oxygenation reserve There appears, therefore, little present need to strive for maximum efficiency of oxygenation

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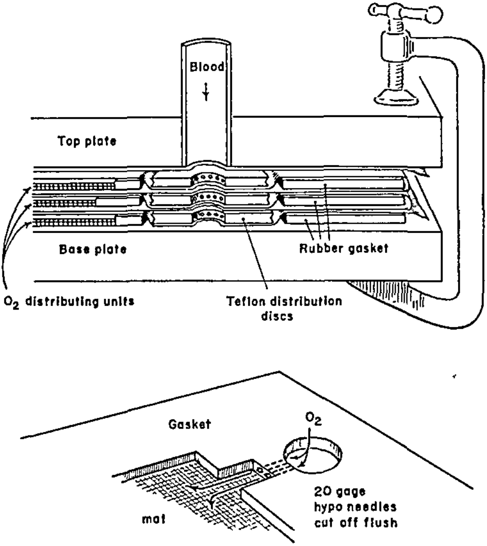
hole). The outside may be cut quite roughly, but the various holes should be made with great care. Standard cork borers are used for the smaller ones, while the 1½ inch diameter holes are cut using a borer made from thin-walled brass pipe. The four small holes along each side determine the position of the guide pins in the base of the lung (Fig. 2). The central rectangles are staggered to allow support for the central inserts shown in Fig. 3, so that there are two types of mats. Further details of construction are shown in the accompanying figures. Acrylic plastic is very satisfactory for the top and bottom plates when chemical sterilizing is available, but if ordinary autoclaving is to be employed, the plates should be made of metal. The original pattern should be kept intact so that additional gaskets can be made when desired. Required materials and the approximate cost are shown in Table VI.



Details of O_2 inflow and outflow

Fig. 3.—The method of blood and oxygen distribution is illustrated. The needles used for oxygen distribution are cut off simply by bending with a pair of pliers. The blood distributing discs are fashioned from 1/16 inch thick Teflon with the cutter used to make the 1½ inch holes in the gaskets. Six radial holes are made in each disc, using a drill about 3/64 inch in diameter. This is most easily done by holding the disc against a stationary drill, such as a drill press, and guiding the drill by keeping one finger on each side of the hole so that lack of alignment can be detected and corrected quickly. After drilling the radial holes, about ⅛ inch is cut from the circumference of each disc with a sharp knife or a second brass cutter. A central hole ½ inch in diameter is then cut. If the drilling is done as the last operation, a burr will result. Pairs of blank discs in several thicknesses are also required (see Assembly). A convenient inlet or outlet tube may be made from a piece of Tygon with a flared end that fits into a blank disc which must then have a ¾ rather than a ½ inch central hole.

TABLE VI. MATERIALS REQUIRED FOR CONSTRUCTION OF A 10 SQUARE METER TEFLON MEMBRANE LUNG

2 sheets Plexiglas (15 in. by 42 in.)	$ 30.00
24 3 in. C clamps	24.00
14 yards 1/16 in. by 36 in. rubber sheeting	33.00
8 36 in. by 36 in. perforated aluminum sheets	18.00
30 yards 24 in. Fiberglas screen	7.00
1 square foot 1/16 in. Teflon	4.00
2 feet 3/8 in. aluminum rod	1.00
Total	$117.00
Each additional mat (0.45 square meter membrane)	2.50
0.0005 in. Teflon* membrane per square meter	4.00

*Dilectrix Corp., Farmingdale, L. I.

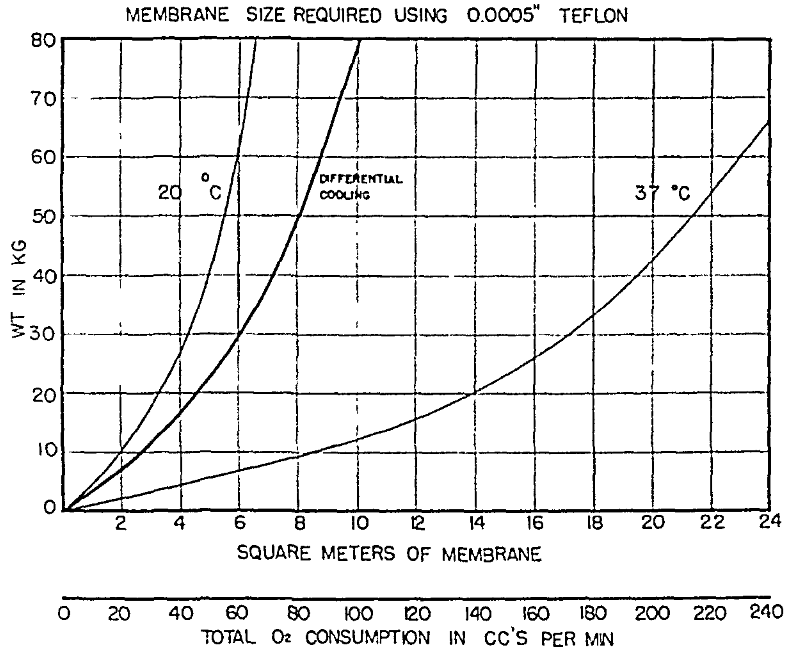


Fig. 4.—The required membrane size is based on the ability of the membrane to transmit carbon dioxide. The amount of membrane indicated provides some oxygenation reserve. This chart may be used for a variety of purposes including determining the requisite blood flow. A flow of 100 c.c. per meter of membrane should fully oxygenate blood even when less than 50 per cent saturated. These flows should prove satisfactory although they are somewhat less than so-called "full flow." (From Peirce et al., J. Tennessee State M. A. 52: 39-44, 1959.)

OPERATION

I. *Assembly.*—

A rubber mat and an insert are placed on the base plate of the lung. Two layers of Teflon membrane are carefully rolled on top of these. Blood distribution discs are placed between the layers of the membrane. A second mat and insert are now placed on top of the Teflon, with care to use a mat that is out of phase with the first one. The process is repeated until the requisite number of meters have been applied (Fig. 4).* The utilization of differential cooling as previously reported will greatly decrease the necessary membrane area.[4] No membrane is placed over the top mat and insert and instead of using an ordinary blood distribution disc, a blank is placed in the large hole of the top mat. Care should be taken that the stacks of distribution discs are the same height as the pile of gaskets, and this can be brought about by having blanks of several thicknesses (produced by sanding down ordinary blanks). An actual cautery is used to perforate the membranes so that gas and blood can circulate. This is best done before applying the top plate. The 24 C clamps are placed symmetrically and tightened firmly. The lung is then tested by placing it on the floor and running normal saline solution into the inlet from a height of 1.5 to 2 meters. As soon as saline appears at the outlet, this is clamped. The saline is allowed to run until it slows down greatly or stops. While this is being done some gas is blown through the lung so that any leakage will be apparent by liquid coming out of the oxygen outlet. Using saline there is practically always slight leakage and a continued drip of up to at least 200 drops a minute is permissible and does not imply any significant blood leak. After testing, the lung is drained by standing it on end.

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*Each mat has an area 10 per cent less than 0.25 meters. For each mat two layers of membrane are used. Roughly, therefore, there is one meter of membrane for each two mats.

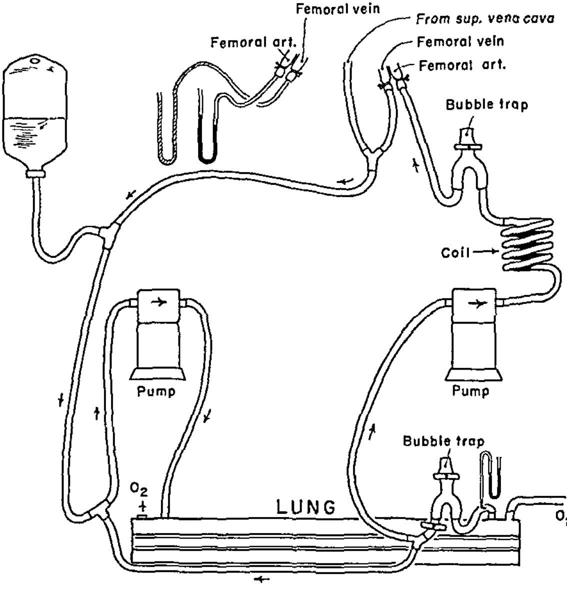

Fig. 5.—The circuit illustrated provides everything essential for a safe perfusion. Monitoring devices, a filter, etc , may be added as desired Note the lack of control devices. (Modified from Peirce et al., J Tennessee State M. A. 52: 39-44, 1959.)

II. *Circuit.*—

A very effective circuit is illustrated in Fig. 5. Two pumps of any satisfactory variety are needed. The lung may be at the same level as the pumps or below, and it makes very little difference. The two bubble traps are necessary for proper priming. They are very simply constructed from ¾ inch Tygon T's. When the blood enters the bubble trap it slows because of the increase in caliber. This, together with the effect of gravity, provides excellent removal of any free bubbles. A stainless steel filter has been used in human beings but not in animals, and we are not convinced that such a filter is necessary or desirable, as very little material tends to collect in it. Temperature is controlled by means of a stainless steel coil or, more recently, by two stainless steel plates held $\frac{1}{16}$ inch apart by a gasket. The heat exchanger can be placed in ice water for cooling or in a warming bath at any temperature up to approximately 40° C. An area of 0.1 meter is entirely adequate for a flow of 1,000 c.c. per minute.

III. *Sterilization.*—

In the research laboratory, although the tubing of the pump circuit has been sterilized with aqueous Zephiran, we have not sterilized the lung itself. For clinical work, we have fortunately had available an ethylene oxide autoclave. The lung and the entire circuit are sterilized as a unit and kept available for use. Steam autoclaving should be entirely satisfactory if metal is used for the lung frame.

IV. *Priming.*—

Using the recommended outlet pressure of about 20 mm. Hg, each meter of lung area requires approximately 120 c.c. of blood to prime it. With abnormally high outlet pressures up to 150 mm. Hg, the priming volume may be more than doubled. The outlet pressure may be monitored with a mercury manometer and controlled with a screw clamp on the outflow limb of the bubble trap. A simple alternative method of pressure control permits elimination of the manometer. The bubble trap is placed about 25 cm. above the outlet of the lung. The screw clamp on its outflow limb is adjusted so that the outflow pressure just supports this 25 cm. column of blood.

The external circuit, consisting of the venous line, shunt, arterial pump, and the remainder of the arterial line, is closed by connecting the venous and arterial limbs which will later be separated and attached to their respective cannulae. In patients, this can be done most conveniently by using a fresh continuous loop of tubing which is then cut and attached to the cannulae after the circuit has been primed. The venous reservoir is placed at the height of the bubble trap in the external circuit. It and the Sigmamotor pump are opened and blood is allowed to fill the external circuit, the lung being excluded. Blood is then circulated with the trap closed until no more air bubbles collect.

The lung circuit is best primed just before it is needed, after the priming of the external circuit. When the lung is below the level of the pumps, initial filling is best accomplished by gravity. As soon as blood appears at the lung outlet, the venous pump is started (the arterial pump is not run at this time) and run until no further bubbles collect in the bubble trap and until the outlet pressure has been properly regulated. If it appears advisable to run gas through the lung during the priming because of slight leakage, it may be best to use air to prevent hyperoxygenation and then to shift to oxygen at the start of the perfusion One liter of gas per meter of membrane provides adequate flow

V *Operation*—

If the venous pressure reservoir is placed at the level of the animal's or patient's venous pressure, no control clamps are required on the lines and the heart lung may be started or stopped by simply turning it on or off The venous pressure can then be kept at a normal level by lowering the reservoir as required

If the apparatus is properly set up with a flow of about 100 c c per meter of membrane, the inlet pressure will vary between approximately 75 and 150 mm Hg There appears to be no advantage in monitoring this pressure As mentioned above, the outlet pressure is important For safety, in case of leakage to prevent gas embolization, it should be kept above the maximum pressure which can be attained in the gas phase Filming, also, appears to be somewhat more even if a positive pressure is kept at the outlet (see Priming)

A shunt is provided between the arterial and the venous lines which serves to balance the flow of the two pumps This prevents any pressure differential and makes it unnecessary to have the pumps exactly the same Hyperoxygenation may be prevented by running the venous pump at a slightly slower rate than the arterial pump This will cause the arterial pump to take up a small amount of venous blood which will then absorb the excess dissolved oxygen If some recirculation through the lung is desired, this is readily provided by running the venous pump at a rate faster than the arterial pump Regulation can be done visually by observing the color of the blood

Small leaks are not infrequent and large leaks may occur occasionally if there is a tear in the membrane or if the lung is put together incorrectly For clinical use, therefore, we recommend that the lung be tested before sterilization (see Assembly) A small leak in no way interferes with proper function and even large leaks are dangerous primarily because of blood loss through them

In the laboratory we have utilized 4 mg per kilogram of heparin in addition to 15 to 20 mg for each 500 c c of priming blood In the human being, we have used only 2 to 3 mg per kilogram There does not appear to be any danger in using extra heparin as it is readily neutralized later There is, however, a danger in using too little heparin as there may be fibrin deposition in portions of the apparatus where the flow is not perfectly streamlined This is very slight in the lung itself

VI *Monitoring*—

As mentioned before, the membrane lung makes it possible to reduce monitoring to a minimum The function of the apparatus is predictable and this eliminates the necessity of following oxygenation, pH, arterial pressure, and many other things which are generally watched carefully In the final analysis everything can be pre set except the venous pressure We believe that this should be followed and regulated

VII. *Re-use of Membrane and Tubing.*—

This has been tried with unsatisfactory results and is not recommended. If the lung is not disassembled, it is impossible to clean it adequately. If it is taken apart, it is almost impossible to avoid tearing the membrane where it has been made adherent by the use of the cautery. In the animal laboratory we have repeatedly re-used the tubing, venous reservoir, and bubble traps, without any apparent difficulty. The circuit is, however, carefully taken apart and all joints cleaned and re-assembled. In the human being, we have preferred to re-use only the special nylon joints and the blood distribution discs. Everything else in the circuit is readily disposable and relatively inexpensive.

SUMMARY

The Teflon membrane lung is the nearest approach to an ideal lung substitute that is presently available. Although it is not so good as the biologic lung, it performs equally as well for the limited demands of intracardiac surgery. When one considers the relative time required for the development of each of these lungs, this is remarkable.

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ANAPHYLACTOID SHOCK DUE TO HOMOLOGOUS BLOOD EXCHANGE IN THE DOG

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During the experimental development of techniques for cardiopulmonary bypass, shock-like states were frequently encountered when dogs were perfused without change in blood volume. Further studies were undertaken to determine the mechanism of these reactions.

METHODS

Five different techniques for blood exchange were used: (1) total cardiopulmonary bypass, (2) transfusion, (3) veno-arterial pumping, (4) left heart bypass, and (5) blood exchange with constant volume.

During 75 total cardiopulmonary bypass experiments in dogs shock was often masked by volume changes. The blood volume of the recipient is necessarily increased by transfusion, so this technique was not extensively studied. In the remaining three methods, extensive blood exchange was produced with closed extracorporeal circuits of fixed volume so that no change in the blood volume of the animal was possible. Veno-arterial pumping consists of the transfer of the superior caval return to the lower aorta without oxygenation,[1] and left heart bypass involves pumping oxygenated blood from the left atrium to the aorta. Blood exchange with constant volume was performed by placing 200 ml. of blood from each donor animal in a closed flask suspended above the recipient and connected to cannulae in the femoral artery and vein. On opening the cannulae, pressure in the flask rose 25 to 30 mm. Hg and blood exchange occurred, the volume of blood in the flask increasing by less than 50 ml.

Mongrel dogs weighing 15 to 25 Kg. were used throughout. Donor blood was obtained from animals lightly anesthetized with 250 to 350 mg. of Pentothal sodium by bleeding from a femoral artery into bottles containing 30 mg. heparin per liter of blood. Subject dogs were similarly anesthetized and secured supine on the operating table. Normal respiration was allowed unless thoracotomy was part of the procedure when artificial ventilation was maintained through an endotracheal tube.

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Arterial pressure was monitored by means of a polyethylene catheter placed in the aortic arch through the femoral artery, and systemic venous pressure by a similar catheter passed into the inferior vena cava via a femoral vein. Portal venous pressure was recorded in some experiments using a catheter inserted through a small abdominal incision into the cranial mesenteric vein. Pressures were recorded with Statham P23D strain gauges and a Cambridge direct-writing recorder.

The extracorporeal circuit for cardiopulmonary bypass consisted of a venous reservoir, a Gibbon-type oxygenator, and rotary pumps. The priming volume of this circuit was about 3,000 ml. and blood from 4 or 5 donors was usually required. The circuits for veno-arterial pumping and for left heart bypass were of 800 ml. capacity and were usually filled with blood from 1 donor, although occasionally 2 donors were needed. In the experiments with simple blood exchange, from 1 to 4 donors were used. With all techniques, blood exchange was begun at between 300 and 600 ml. per minute. Various courses were followed subsequently. When shock was evident, exchange was sometimes stopped so that the hemodynamic changes could be observed without disturbance; in other studies extracorporeal flow was maintained.

The effects of intravenous injection of *Escherichia coli* endotoxin in doses from 1 to 7 mg. were observed in similar preparations.

RESULTS

The incidence of shock was similar with each of the techniques for blood exchange without change in volume (Table I).

TABLE I. INCIDENCE OF SHOCK FOLLOWING BLOOD EXCHANGE

EXPERIMENTAL PROCEDURE	NUMBER OF EXPERIMENTS	INCIDENCE OF SHOCK
Veno-arterial pumping	55	17
Left heart bypass	8	3
Constant volume blood exchange	47	21
Totals	110	41

Simple transfusion with 200 ml. of homologous donor blood caused shock in 3 out of 6 trials. Exchange using autogenous blood produced no effect, although in 10 of the 16 trials the blood was deliberately poorly heparinized and contaminated. The incidence of shock increased considerably when blood from more than 1 donor was used to fill the extracorporeal circuit (Table II). In total cardiopulmonary bypass, where blood from 4 or more animals was used to prime the system, evidence of shock appeared as arterial hypotension, reduced venous return or blood transfer from extracorporeal circuit to subject animal in all cases in which adequate data were available for analysis.

An abnormal reaction to blood exchange was usually apparent in 1 minute as a sharp rise of portal venous pressure associated with distention of the liver and the portal venous radicals. The subsequent course was similar whether blood exchange was discontinued or maintained, providing the volume of blood

TABLE II. RELATION BETWEEN NUMBER OF DONORS AND INCIDENCE OF SHOCK
(114 EXPERIMENTS WITH EXTRACORPOREAL CIRCUITS OF FIXED VOLUME)

NUMBER OF DONORS	NUMBER OF EXPERIMENTS	INCIDENCE OF SHOCK
1	86	25
2 or more	28	17

in the animal and in the extracorporeal circuit remained constant. The systemic venous pressure was unchanged but the venous return diminished rapidly and there was a corresponding fall in artérial pressure Maximal pressure changes were attained in 3 to 5 minutes, the portal venous pressure reaching 40 mm. Hg in the more severe cases and the mean arterial pressure falling to 20 mm. Hg (Fig. 1, *A*). Slight degrees of shock, on the other hand, produced a rise of portal venous pressure of only 1 or 2 mm. Hg, the small fall in arterial pressure being difficult to recognize. During the next hour the pressures returned almost to normal levels, although portal distention was still apparent.

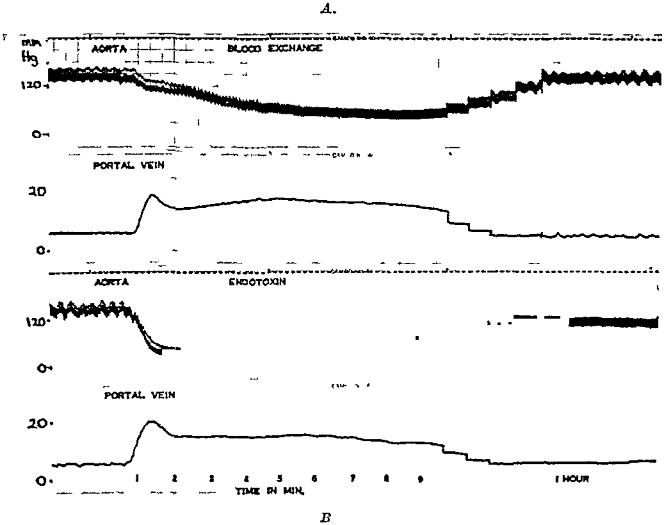

Fig 1—*A*, Effect of homologous blood exchange on the arterial and portal venous pressure with an extracorporeal circuit of fixed volume

B, Similar changes in arterial and portal venous pressure following the injection of *Esch coli* endotoxin

If bypass was continued and the volume of the extracorporeal circuit kept constant, the reduction in venous return necessarily limited the extracorporeal flow. In the less severe degrees of shock, the venous return and arterial pressure could be maintained by allowing the animal to take up blood from the extracorporeal circuit (Fig. 2). Perfusion could then be continued at acceptable extracorporeal flow rates, but only at the expense of further distention of

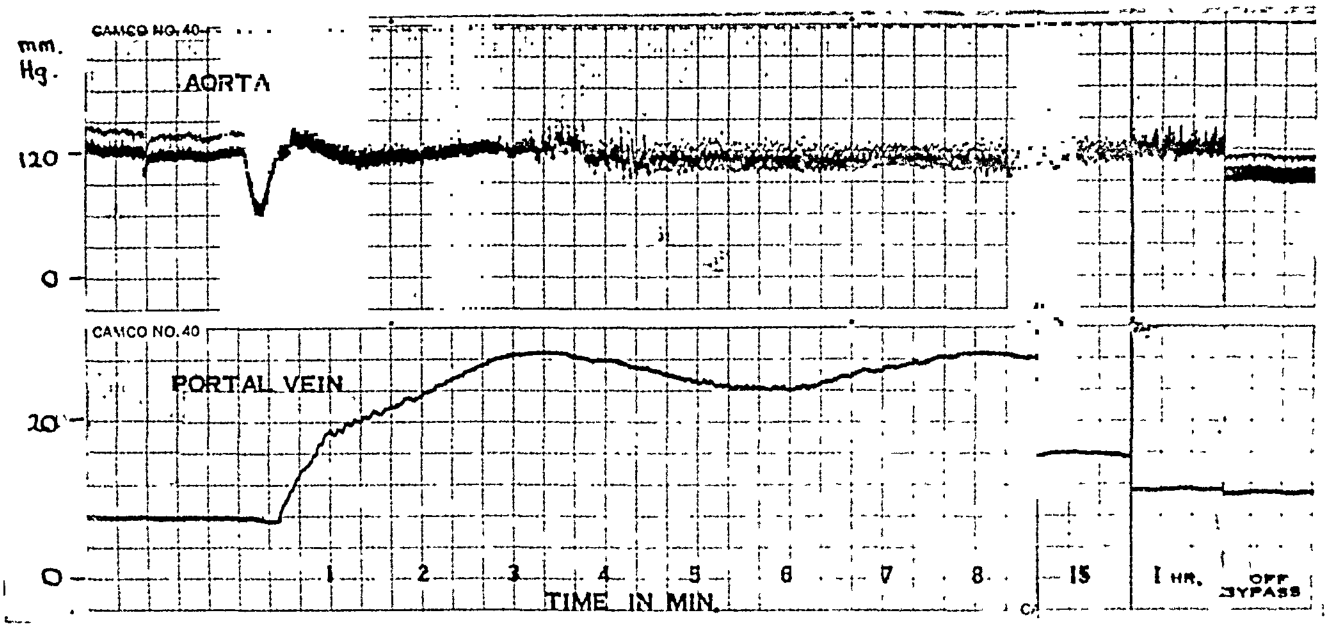

Fig. 2.—Effect of homologous blood exchange on the arterial and portal venous pressure in total cardiopulmonary bypass. The animal was allowed to take up blood from the extracorporeal circuit from the onset of blood exchange.

the portal system. Some animals tended to recover control of their vascular volume toward the end of a 1-hour period of perfusion and returned some blood to the extracorporeal circuit. More often, however, there was a serious fall in blood pressure at the termination of bypass, the excess blood was retained and the animals failed to recover consciousness.

In an attempt to localize the agent in blood responsible for the shock reaction, two experiments were performed in which the donor cells and plasma were separated by centrifuging. Blood exchange with donor cells suspended in saline produced no ill effect, but shock resulted from exchange using the plasma from these animals.

Injections of *Esch. coli* endotoxin, in varying dosage, produced hepatic engorgement and changes in the portal venous and systemic arterial pressures similar in degree and timing to those resulting from blood exchange (Fig. 1, *B*).

DISCUSSION

A number of studies of blood transfusion in normal dogs have shown that added plasma is rapidly lost from the circulation.[2-5] In one of these studies, 6 out of 34 dogs showed urticaria and a fall in blood pressure.[3] Other reports of the effects of plasma transfusion in dogs indicate that urticaria is almost invariable.[6, 7] Similar reactions were found during experimental hemodialysis by the Mayo Clinic group.[8, 9] A fall in blood pressure with bradycardia, respiratory depression, and urticaria was noted at the onset of hemodialysis in 27 of 37 dogs and was associated with a mortality of more than 30 per cent. These reactions were eliminated by priming the extracorporeal circuit with autogenous blood, saline solution, or some dextrans. More severe changes of this type have been found following plasma infusion in the adrenalectomized dog.[10, 11] Urticaria is generally much less prominent in experiments performed under anesthesia.[7, 11]

It has been shown that plasma reactions are not related to the blood group of the dogs or the presence of plasma iso-agglutinins.[7, 8] Natural isoantibodies are found in only about 15 per cent of random dogs, and are mostly of low potency.[12, 13] The suggestion that incipient coagulation due to suboptimal heparinization of blood is responsible for these changes after transfusion[14] is not supported in our present studies, as poorly heparinized autogenous blood did not produce shock.

When reactions to plasma transfusion were first noticed, their similarity to histamine effect[7, 11] and to anaphylactic shock[6] was remarked. Anaphylaxis in the dog is associated with an acute fall in blood pressure and elevation of portal venous pressure with segregation of blood in the portal venous system and liver.[15, 16] The mechanism has been a subject for considerable discussion[17-19] but it seems likely that diffuse spasm of the smooth muscle in the hepatic venous system is mainly responsible.[20] There is good evidence that anaphylactic shock is due to histamine release.[21-24]

Anaphylactoid shock, that is, a syndrome resembling anaphylaxis but not associated with demonstrable previous sensitization, has been found frequently in response to the injection of a wide variety of substances.[25, 26] These include colloidal iron, peptone, rattlesnake venom,[27] hydatid fluid,[28] and Ascaris extracts.[29] The endotoxin produced by gram-negative bacteria has a similar effect and has been investigated in detail.[26, 30, 31]

The similarity of the changes described here with homologous blood exchange to those described in anaphylaxis in dogs is apparent, and we have been able to reproduce most of the effects by the injection of *Esch. coli* endotoxin. It seems, therefore, that there is an agent in dog blood which produces anaphylactoid shock. The effect is evident in less than one third of donors, but, when mixed blood from many donor animals is used, the incidence of shock is considerably greater. Our fractionation studies suggest that a plasma factor is responsible, although other workers have reported reactions to washed red cells.[6, 7]

The resemblance of the effects of gram-negative bacterial endotoxins to the changes that follow blood exchange has lead to the suggestion that endotoxin is present in donor blood as a result of bacteremia when the animal is exsanguinated. However, reactions were no less frequent in experiments in which only 200 ml. of blood was taken from each donor.

It has been suggested[32] that reactions of this type occurring during the course of cardiopulmonary bypass were due to acidosis. Similar changes have been produced by CO_2 retention or hydrochloric acid infusion. The shock-like effects reported here, however, were evident at the onset of blood exchange before acidosis had occurred. This does not exclude the possibility that acidosis itself may produce shock.

Anaphylactoid responses to blood exchange may interfere considerably with the interpretation of physiologic studies in dogs. Conclusions based on experiments involving blood exchange in which this factor is not recognized must be interpreted with caution. The more severe varieties of anaphylactoid shock will be detected easily by observation of the arterial pressure during the first few minutes of blood exchange, providing the volume of blood in the extracorporeal circuit is kept constant. However, minor variants may be missed unless the portal venous pressure is measured. In cardiopulmonary bypass, detection of these effects is especially difficult as venous return and perfusion can be maintained if the animal is allowed to take up blood from the extracorporeal circuit.

A preliminary test transfer of 200 ml. of donor blood can be used to determine whether an anaphylactoid reaction will occur. If shock is produced, an interval of 1 hour will allow the arterial and portal venous pressures to return to normal. Useful experimental data can then be obtained, but many of the effects of shock on the circulation and the liver probably persist.

It has been reported that antihistamines[7, 11] or adrenergic blockade[8, 9] will reduce the effect of plasma infusion, and large doses of hydrocortisone have been shown to prevent endotoxin shock.[33] These findings suggest that animals can be protected against reactions to blood exchange, but the large doses of potent agents required may produce other undesirable effects.

SUMMARY AND CONCLUSIONS

1 Blood from about a third of donor dogs produced a shock like effect in the recipient animal The incidence is greater when mixed blood from a number of donors is used

2 The onset of shock is characterized by a rapid rise in portal venous pressure with distention of the liver and portal system

3 If the volume of the extracorporeal circuit is fixed, the arterial pressure falls as the portal venous pressure rises, suggesting that sequestration of blood is occurring in the portal system The venous return and, consequently, the extracorporeal flow are reduced in these circumstances

4 The portal venous and arterial pressures tend to recover in the course of an hour but the portal congestion persists

5 If the animal is allowed to take up blood from the extracorporeal circuit, the arterial pressure and venous return are better maintained, but sequestration in the portal system is accentuated

6 The syndrome is similar to the effects of anaphylaxis in the dog

7 Reactions of this type following blood exchange may interfere with the interpretation of experimental studies in dogs

8 A preliminary test exchange with 200 ml of donor blood can be used to determine whether shock will occur in any particular experiment

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THE EFFECTS OF ANAPHYLACTOID SHOCK FROM BLOOD EXCHANGE ON CARDIOPULMONARY BYPASS IN THE DOG

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INTRODUCTION

During 75 cardiopulmonary bypass experiments in dogs it became apparent that there was a tendency for the animals to take up blood from the extracorporeal circuit. A study of the effects of homologous blood exchange in dogs[1, 2] demonstrated that blood from approximately one third of random donors produced a state resembling anaphylactic shock, with sequestration of blood in the liver and portal venous system. The present study was undertaken to assess the effects of anaphylactoid shock resulting from blood exchange on the course of cardiopulmonary bypass in the dog.

METHODS

Mongrel dogs weighing 15 to 25 Kg. were used throughout. Donor blood was obtained from animals lightly anesthetized with Pentothal (15 mg. per kilogram body weight), by arterial exsanguination into bottles containing 30 mg. of heparin per liter of blood. Subject dogs were anesthetized with Nembutal (25 mg. per kilogram body weight) and secured supine on the operating table. Aortic blood pressure was monitored by a polyethylene catheter in the femoral artery, and portal venous pressure by a catheter placed in the cranial mesenteric vein through a small abdominal incision.

The effects of blood exchange were investigated using a simple extracorporeal system in which 200 ml. of blood from each donor was suspended in a liter flask above the animal and connected to cannulae in a femoral artery and vein. When the cannulae were opened, pressure in the flask rose 25 to 30 mm. Hg and blood exchange occurred, the volume of blood in the flask increasing by less than 50 ml. Blood samplers were obtained when the shock was maximal (3 to 5 minutes). Blood exchange was then discontinued and further samples taken after an hour.

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Cardiopulmonary bypass was performed with a venous reservoir, a rotating disc oxygenator, and a pump with ball valves at each end of a silicone rubber chamber driven by pulses of compressed air.[3] Cannulation was performed without opening the thorax. The venous cannulae were inserted through a femoral vein into the inferior vena cava and through the right external jugular vein to the superior vena cava. The arterial cannula was placed in a femoral artery. Side arms on each venous cannula enabled blood samples to be obtained, and mixed venous and arterial samples were available from the inflow and outflow lines of the oxygenator. When total bypass was performed, an endotracheal tube was inserted and ventilation maintained with a respirator. The right chest was then opened and ligatures placed around the venae cavae proximal to the cannulae. The coronary venous return was allowed to pass through the heart normally. Cardiopulmonary bypass was maintained for 60 minutes in each animal and blood samples were obtained at 20-minute intervals. Extracorporeal flow was measured by determining the time taken for the volume of the venous reservoir to increase 100 ml. when its outflow line was temporarily occluded.

Pressures were measured with Statham P23D strain gauges and a Cambridge direct writing instrument. Blood oxygen and CO_2 contents were measured,[4] as were the plasma pH, hematocrit, electrolytes, lactate,[5] and pyruvate.[6] The oxygen saturation was expressed as a percentage of the hemoglobin capacity without correction for the oxygen in solution. A nomogram[7] was used to derive the pCO_2 and buffer base.

RESULTS

Twenty-two animals were studied and five different types of experiments were performed (Table I). Shock was evident in all bypass studies, and blood exchange experiments that did not show shock were excluded.

TABLE I

A. Blood exchange alone	(4 animals)
B. Blood exchange followed after 1 hour by total bypass without change in blood volume	(4 animals)
C. Total bypass without change in blood volume	(5 animals)
D. Total bypass with hypervolemia	(5 animals)
E. Partial bypass with hypervolemia	(4 animals)

In all experiments the blood pressure fell sharply, sometimes to less than 50 mm. Hg, and the portal venous pressure increased (average rise from 7 to 22 mm. Hg), the liver and portal venous radicals becoming distended. These changes began approximately 1 minute after the onset of blood exchange and were maximal in 3 to 5 minutes.

In Groups A, B, and C (13 animals) the effects of shock were studied. Apnea occurred during the period of shock in some animals and the arterial oxygen saturation fell correspondingly. There was a profound fall in venous oxygen saturation during shock, the arteriovenous oxygen difference reaching nearly double the control value. The hematocrit tended to rise as soon as shock was apparent and this increase was greater after 1 hour. Buffer base fell nearly 3 mEq./L. on the average and there was a rise of approximately 1 mEq./L. in the blood lactate. The sodium and chloride levels both rose about 1.5 mEq./L., but there was no significant change in the plasma potassium (Table II).

TABLE II Effects of Anaphylactoid Shock From Blood Exchange (13 Animals) and of Cardiopulmonary Bypass (18 Animals)

	Mean control values	Shock	Recovery	Bypass		
Time (min.) from onset of blood exchange		3 to 5	60	20	40	60
Hematocrit (%)	51	+1.3	+2.6	+1.7	+2.8	+1.6
Buffer base (mEq./L.)	45	−2.9	−2.4	−3.4	−6.0	−7.3
Na + (mEq./L.)	154	+0.8	+1.6	−2.2	−2.6	−0.4
Cl − (mEq./L.)	109	+1.8	+1.4	−0.1	+2.1	+2.6
K + (mEq./L.)	4.3	+0.1	−0.3	−0.4	−0.7	−0.6
Lactate (mEq./L.)	2.1	+1.7	+0.8	+1.5	+2.1	+2.7
Pyruvate (mEq./L.)	0.15	+0.1	+0.05	+0.05	+0.1	+0.1

The changes resulting from blood exchange associated with bypass were studied in Groups B, C, D, and E (18 animals). Those perfused without change in blood volume showed a fall in flow and arterial pressure at the onset of blood exchange, but when the animal was allowed to take up blood from the extracorporeal circuit the fall in arterial pressure was less and satisfactory venous return and bypass flow were maintained. The volume change ranged from 400 to 1,400 ml. The optimal bypass flow in each animal was between 0.5 and 1.6 L./min./M.^{2} (mean 1.0 L./min./M.^{2}). The arterial oxygen saturation was well maintained but there was a considerable increase in the arteriovenous oxygen difference, both in partial and total bypass experiments. The hematocrit rose by approximately the same amount as in shock. A metabolic acidosis developed during bypass, the buffer base falling by 7 mEq./L. and the blood lactate rising by 2.5 mEq./L. over a period of an hour. The pyruvate changes were similar to the lactate but on a much smaller scale. The sodium levels fell by 2 mEq./L. at 20 and 40 min., returning to normal at 60 min. Chloride levels rose by 2 mEq./L. at 40 and 60 min. There was a fall of about 0.5 mEq./L. in the plasma potassium during the period of bypass (Table II).

In two additional partial bypass studies, the effects of blood exchange were modified. In 1 animal, a side to side anastomosis was made between the portal vein and the inferior vena cava before bypass was begun. There was no rise in portal venous pressure or fall in arterial pressure on blood exchange and the venous oxygen contents were unchanged, although the liver became considerably distended. In the second animal, 400 mg. of diphenhydramine was given. The portal venous pressure rose at the onset of bypass but there was no fall in arterial pressure or venous oxygen content.

The metabolic effects were similar in both these animals (Table III). The hematocrit fell slightly as did the buffer base. The lactate rose 2 mEq./L., the pyruvate 0.2 mEq./L., after an hour. The electrolyte changes were similar to those found in the other experiments, the sodium falling 3 mEq./L., the potassium 0.5 mEq./L., and the chloride rising 3 mEq./L.

TABLE III. EFFECTS OF BYPASS IN 2 ANIMALS WITH MODIFIED RESPONSE TO BLOOD EXCHANGE

	MEAN CONTROL VALUES	BYPASS		
Time (min.) from onset of blood exchange		20	40	60
Hematocrit (%)	51	− 0.3	− 0.7	− 1.3
Buffer base (mEq./L.)	44	0	− 0.2	− 0.8
Na + (mEq./L.)	154	− 1.0	− 3.0	− 3.0
Cl − (mEq./L.)	114	0	+ 1.5	+ 3.0
K + (mEq./L.)	3.3	− 0.1	− 0.6	− 0.5
Lactate (mEq./L.)	2.3	+ 1.7	+ 1.0	+ 2.0
Pyruvate (mEq./L.)	0.1	+ 0.15	+ 0.15	+ 0.2

A further experiment was performed in which the extracorporeal circuit was filled with gelatin solution. There was no fall in arterial pressure or elevation of portal venous pressure following bypass in this animal.

DISCUSSION

Unusual responses to transfusion of various blood components have been found in dogs,[8-17] and shock-like changes have been reported by many workers with the extracorporeal circulation. The release of toxin from cellophane,[18] incipient coagulation due to suboptimal heparinization,[19] and the absence of pulsatile flow[20] have been suggested as possible mechanisms but seem unlikely in view of subsequent work.[1, 2, 14, 21] Experimental studies[1, 2] indicate that anaphylactoid shock is produced by 200 ml. of plasma from approximately one third random canine donors. In total cardiopulmonary bypass, where the extracorporeal circuit has a large volume, blood from 3 or more donors is needed to fill the circuit. In these circumstances there was evidence of shock in all our procedures for which adequate data were available. No shock occurred when the circuit was primed with gelatin, and the response was considerably modified by preliminary portocaval anastomosis and by diphenhydramine.

Anaphylactoid shock from blood exchange has a considerable effect on the course of cardiopulmonary bypass in the dog. Sequestration of blood in the liver and portal venous system leads to a reduction in venous return, and so restricts the extracorporeal flow. Systemic perfusion is reduced and the blood pressure falls. If the animal is allowed to take up blood from the extracorporeal circuit, the venous return and blood pressure may be maintained, but at the expense of a further increase in hepatic and portal venous congestion.

Metabolic acidosis during cardiopulmonary bypass is, at least in part, the result of accumulation of acid metabolites due to incomplete oxygenation. In the present study the increase in blood lactate accounts for about a third of the fall in buffer base. There is also an increase in blood pyruvate but the changes are trivial. However, it is probable that lactate is only a small and variable fraction of the total organic acid accumulation.[21]

A similar acidosis occurs as a result of anaphylactoid shock from blood exchange which is an integral part of the response to bypass in the dog. Both in isolated shock and in bypass, direct measurement and the changes in arteriovenous oxygen difference indicate that systemic blood flow falls considerably. Decreased tissue perfusion may be responsible for the acidosis. The absence of metabolic acidosis during veno-arterial pumping,[23] in which the lower part of the body is perfused with unsaturated blood and total systemic blood flow is unchanged, suggests that tissue hypoxia is not the causative factor.

The hepatic congestion produced by the anaphylactoid response to blood exchange is present during bypass and may be a factor in the production of acidosis. Even when an interval of 1 hour was allowed after blood exchange, considerable portal congestion persisted. Anaphylactoid shock from blood exchange is associated with a rise in hematocrit and plasma electrolyte levels which suggests hemoconcentration and loss of water to the cells. During cardiopulmonary bypass there is a fall in plasma sodium and potassium and a rise in chloride indicating a major electrolyte shift tending to produce acidosis. Similar changes were noted by Pontius and his associates.[24]

In the two bypass experiments in which the anaphylactoid response was modified, systemic perfusion was maintained near normal levels. Although the electrolyte changes and accumulation of organic acids were similar to those found in other bypass studies, there was little impairment of buffer base, suggesting that shock from blood exchange or inadequate systemic perfusion may produce metabolic acidosis in other ways.

The relation of anaphylactoid shock in dogs to hypotension or acidosis in human extracorporeal circulation is problematical. Hemodialysis studies at the Mayo Clinic suggests that similar reactions may occur in a number of human cases of massive blood exchange.[13] There is evidence that a vasoconstrictor mechanism exists in the hepatic veins of man,[25] so that similar reactions to those described here in dogs may be of importance in human work.

SUMMARY AND CONCLUSIONS

1. Blood from about one third of donor dogs produces anaphylactoid shock in the recipient animal.

2. Anaphylactoid shock is an integral part of the response of the dog to cardiopulmonary bypass as a large volume of blood from many donors is used to fill the extracorporeal circuit.

3. Anaphylactoid shock in the dog is associated with sequestration of blood in the liver and portal venous system. Bypass flow and arterial pressure fall, but the changes are less evident if the animal is allowed to take up blood from the extracorporeal circuit.

4. Accumulation of organic acids was found in anaphylactoid shock, either occurring alone or in association with cardiopulmonary bypass. Systemic perfusion was below normal levels in both situations. Cardiopulmonary bypass was also associated with an electrolyte shift producing metabolic acidosis.

5. Modification of the anaphylactoid response by a portocaval anastomosis, or by diphenhydramine, allowed bypass without a reduction of systemic blood flow. Although there was organic acid accumulation and similar electrolyte changes to those found in other bypass studies, there was little metabolic acidosis in these experiments.

6. Responses to massive blood exchange similar to those described here may be of importance in human work.

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VENO-ARTERIAL PUMPING IN NORMAL DOGS AND DOGS WITH CORONARY OCCLUSION

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PARTIAL BYPASS of the heart appears to be a reasonable approach to the problems of coronary shock and intractable heart failure. If partial perfusion of the body can be instituted safely for prolonged periods, the decreased work required of the heart may allow an infarcted or failing heart to maintain adequate coronary flow and subsequently to recover.

Stuckey and his co-workers[1] reported their experience in the use of a heart-lung machine in patients with severe myocardial infarction. We wondered whether a pump without an oxygenator would be of clinical value in similar patients. We theorized that a pump alone might relieve the heart of some of its work, help maintain or improve coronary flow, and be available for emergency use at very short notice. It was hoped that the reduced cardiac output through the lungs would be sufficient to accomplish satisfactory oxygenation of blood going to the heart, brain, and kidneys and that the lower part of the body would withstand the relative anoxia. Hamer and his associates[2, 3, 4] have recently reported their results with arterial perfusion of venous blood. They proposed its use in patients with heart failure and myocardial infarction. We felt that our experimental data, however meager, should be made immediately available in order to emphasize the potential dangers of veno-arterial pumping in patients with myocardial infarction.

MATERIALS AND METHODS

Jugular vein blood was pumped into a femoral artery with a Sigmamotor pump in 14 dogs. The perfusion circuit generally established is shown in Fig. 1. Whenever the venous blood was pumped into the brachial or carotid artery instead of the femoral artery, the animal responded poorly, due to the perfusion of the heart and brain with poorly oxygenated blood.

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Sampling catheters were placed in the aorta at the level of the diaphragm and in the aortic arch. This was accomplished via the femoral and carotid arteries, respectively. The blood pressure was monitored with a mercury manometer by means of a cannula in the brachial artery. The perfusion rate was obtained by measuring the decrease in blood volume within the graduated collecting reservoir over a 15-second period with the inflow tubing occluded. An alternative method was to divert the venous drainage into a graduated cylinder for a 15-second period. The two methods checked closely.

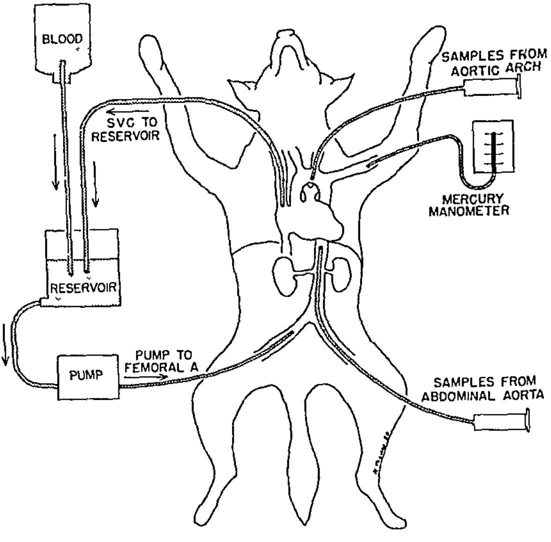

Fig. 1 —Diagram showing perfusion circuit and location of sampling catheters.

Most of the animals were anesthetized with intravenous Nembutal and the trachea was intubated. This permitted ventilation with a 95 per cent oxygen-5 per cent carbon dioxide mixture through an Emerson intermittent positive pressure respirator. While on this mixture, the blood carbon dioxide usually remained within normal limits. Although a few animals were perfused under morphine and local anesthesia, having the animal quieter under barbiturate was a great advantage and therefore was preferred.

Most of the experiments were not conducted with sterile precautions and the animal was later sacrificed. Heparinization was accomplished with a dose of 1 mg. per pound. The rate of perfusion was determined by the maximum rate of venous flow that could be obtained under different experimental conditions.

In order to produce coronary artery occlusion, a No. 1 silk ligature was loosely looped about the anterior descending branch of the left coronary artery

(LAD) with a surgeon's knot and the ends of the ligature were buried subcutaneously several weeks in advance. When occlusion was required, the two ends of the suture were exposed and pulled taut. The effectiveness of the acute coronary occlusion was checked by electrocardiographic tracings and later postmortem examination.

RESULTS

In 10 normal dogs, 15 to 25 kilograms, veno-arterial pumping with unoxygenated blood was performed for periods varying from 3 to 5 hours at rates varying from 300 to 1,000 ml. per minute. Once the technical problems of pumping were mastered, survival of the animal could be expected. Our oxygen saturation studies indicated that the venous blood pumped into the femoral artery did not lower the oxygen saturation of the blood above the level of the renal arteries. This held true only as long as the animal's blood pressure was maintained within normal limits. Long-term survival was observed in the only dog pumped under sterile precautions. Experiments on the other 9 dogs were terminated at the end of the perfusion period.

In 4 dogs, coronary artery occlusion was produced prior to starting the pump. In each instance the blood pressure was satisfactory for 30 minutes until the pumping with venous blood began. Within 10 minutes thereafter, the blood pressure fell precipitously in all 4 instances. Cyanosis of the mucous membranes of the head was observed. Blood pressure was temporarily restored by blood transfusion and norepinephrine, in 2 of the 4 animals. Maximum flow rates of 100 to 600 ml. per minute were obtained. Death occurred at 8, 10, 15, and 60 minutes after instituting pumping. Electrocardiographic examination and postmortem examination indicated that 2 of these animals had had an acute coronary artery occlusion produced by the previously placed ligature. The other 2 dogs had older occlusions, apparently produced sometime following the placement of the ligature several weeks previously. Their performance on veno-arterial pumping was no better than the 2 dogs with fresh occlusions, 1 of which survived for 60 minutes.

DISCUSSION

The results obtained suggest that a partial bypass with unoxygenated blood may be tolerated by a dog with a normal heart. A line of demarcation between oxygenated and unoxygenated blood can be obtained near the level of the diaphragm. This point was also demonstrated by Hamer and his co-workers[2] who used a radiographic technique. However, when a fresh or recent coronary artery occlusion exists, the dogs do not tolerate veno-arterial pumping. Presumably, the myocardium no longer has the ability to maintain a satisfactory cardiac output against the action of the pump. Venous blood perfuses the upper arterial tree and rapid deterioration in the condition of the animal ensues. Dogs which had satisfactorily compensated for a coronary artery occlusion were promptly thrown into irreversible shock when venous blood was pumped into their arterial systems via the femoral artery.

We have had no experience with animals in heart failure. Theoretically, veno-arterial pumping might be of benefit in patients with right heart failure.[5] The failing right ventricle would be relieved by continuous phlebotomy while the pump returned the blood to the arterial side. This would increase the load on the left ventricle but also would increase the coronary artery perfusion. However, the newer heart-lung machines are being improved in simplicity and efficiency to the point where there seems to be little advantage or justification for using the pump alone.

SUMMARY

Venous blood was pumped into the femoral artery of 10 normal dogs for 3 to 5 hours without serious adverse effect. When fresh or recent coronary artery occlusion was produced in 4 additional dogs, the same procedure produced irreversible shock within 10 minutes. It is concluded that veno-arterial pumping in patients with coronary artery occlusion would be harmful rather than beneficial.

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POTASSIUM ION AS A CARDIOPLEGIC AGENT IN TOTAL CARDIAC BYPASS AND DURING HYPOTHERMIA WITH CORONARY PERFUSION

An Experimental Study

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THE REVERSIBILITY of potassium induced cardioplegia does not follow a systematic pattern. Its unpredictability places it in the category of methods requiring discriminative and judicious application. Because of the limited physiologic knowledge available, we have attempted to elucidate information concerning the fate of this ion when used in cardioplegia. In a previous report[5] from this laboratory, it was noted in normothermic and hypothermic animals that (a) the reversibility of cardioplegia was not uniformly related to the amount of potassium injected or to its concentration in the myocardium, (b) "washing out" potassium was not synonymous with resumption of normal rhythm, and (c) hypothermic animals subjected to such arrest suffered much greater mortality than was observed in a comparable group of normothermic dogs. Prior digitalization of the former group, however, had a beneficial effect.

In a continuation of these studies, the metabolism of potassium during cardioplegia has been observed in dogs subjected to total cardiac bypass and in hypothermic animals with venous inflow occlusion and coronary perfusion. The purpose of this paper is to present information obtained concerning the fate of this ion under these circumstances.

METHOD

Thirty-two mongrel dogs of both sexes, weighing 15 to 25 Kg., were equally divided into two groups—Group I comprised those having total cardiac bypass, and Group II those having hypothermia with coronary perfusion. All animals were anesthetized with intravenous thiopental, 35 mg. per kilogram, and supplemented with ether when additional anesthetic was required.

A bubble oxygenator and Sigmamotor pump were employed for the achievement of total cardiac bypass in Group I animals. Body temperature was continuously monitored and maintained at normothermic levels. The extracorporeal

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system was primed with heparinized blood (18 mg. of heparin per 500 ml.) which had been collected in siliconized bottles from healthy dogs the day of the experiment. Following insertion of two Tygon catheters (3⁄8 inch internal diameter) into the venae cavae through the right auricular appendage and through a purse-string suture in the wall of the right atrium, they were joined to a Y tube and venous blood was collected by gravity into a reservoir, 50 cm. below the level of the right atrium. The arterial line was connected to a No. 16 plastic catheter which was inserted into either the femoral or the subclavian artery. Pump flow averaged 65 ml. per kilogram per minute.

Animals in Group II were made hypothermic by surface cooling in a fashion precisely as described many times previously from this laboratory.[3-5] They were maintained at a body temperature of 28° to 29° C. during the experiment. Artificial respiration was carried out by means of an automatic respirator. Coronary perfusion during the period of venous inflow occlusion was accomplished by connecting a reservoir of heparinized blood maintained at 37° C. to a No. 16 plastic catheter which was inserted via the subclavian artery into the ascending aorta. Constant flow (avg. 100 ml./min.) and pressure (130 mm. Hg) of the perfusate were maintained.

During venous inflow occlusion, coronary sinus blood was withdrawn from the right atrium in Group I by needle puncture, and in Group II by a catheter inserted into the atrium through the jugular vein. This served to prevent distention of the right heart as the result of the coronary perfusion, to permit blood sampling for quantitative study, and to remove the potassium solution used to induce standstill which, after traversing the coronary tree, had accumulated in the right atrium.

The rest of the protocol was essentially similar for both experimental groups and was identical with that described in our prior report.[5] Bilateral thoracotomy was performed through the fourth intercostal space Following venous and aortic occlusion, cardiac arrest was produced by the injection of a solution of 25 per cent potassium citrate (2 ml.), normal saline (18 ml.), and heparin (0.5 ml.) containing K^{42}.* Prior to injection, the radioactivity of the solution was determined by placing the loaded syringe beneath a scintillation tube. Following the induction of cardiac standstill and during the entire process of resuscitation, radioactivity of the heart was recorded. A sodium iodide, thallium detector for gamma rays (Nuclear Chicago), which fed into a count rate meter and this, in turn, into a linear and logarithmic recorder, was used for the purpose. During standstill, a piece of myocardium, M_1, was removed from the right ventricular wall for later study. After 6 minutes of venous inflow occlusion in Group II, coronary perfusion, which was maintained during this period, was stopped, caval clamps were released, and cardiac massage was begun. When a stable plateau of activity over the heart was observed, a second sample of myocardium, M_2, was removed from the right ventricle and the experiment was terminated by sacrificing the animals.

At autopsy, the heart was removed and its radioactivity was again determined to eliminate all possibility of an overlapping of counts from organs

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*From Oak Ridge National Laboratory (10 millicuries in approximately 1 ml. of solution).

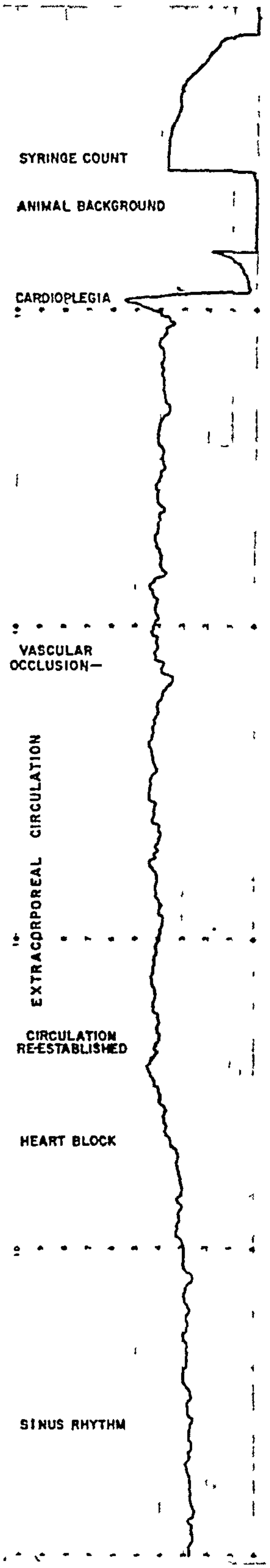

Fig. 1.—K^{42} (counts/min.) in the heart during and after cardioplegia with total cardiac bypass. (Read from right to left.)

other than the heart which might have occurred in vivo. The left and right ventricular myocardium, atria, and the septum were separated from each other and were individually examined for radioactivity. For that purpose, a subminiature probe counter tube* was employed. This is a stainless steel thin-walled counter which has a small sensitive volume and generates pulses, the amplitude of which are large enough to drive a scaler without need of a pre-amplifier. The probe was connected to a scaler and this in turn to a continuous graph recorder. It was introduced for a distance of 1 cm. into the depth of the myocardial segments. Separate recordings were made from the upper, middle, and lower thirds of the ventricular septa. Pieces of lung, liver, and kidneys were taken for determination of radioactivity. All samples were dried for 24 hours in a 100° C. forced draft oven prior to counting. Serial determinations of serum potassium, blood pH, and K^{42} activity in peripheral blood were made before and after cardiac standstill. The electrocardiogram was continuously monitored in all experiments.

RESULTS

Total Cardiac Bypass (GROUP I).—

The 16 animals in this group were subjected to 20 minutes of cardiac bypass at the onset of which cardioplegia was produced by an average of 12 ml. of the potassium solution having an activity of 5.1 million counts per milliliter per minute. A typical tracing depicting the radioactivity of the heart during and after cardioplegia with bypass is shown in Fig. 1. The sharp ascending limb, due to the proximity of the loaded syringe to the heart during injection, was followed by a descending slope associated with withdrawal of the syringe. Radioactivity remained fairly constant during the period of vascular occlusion and cardiac bypass. Upon removal of the aortic clamp a gradual descent of the tracing was observed. In this group, during occlusion an average of 3,200 counts/min. (100 per cent) was obtained by scanning over the heart. Immediately after removal of the clamps, activity was found to be 97 per cent (3,100 counts/min.) of the counts obtained during total bypass. At the onset of cardiographic evidence of electrical activity, the radioactivity was 2,900 counts/min. (89 per cent), and by the end of the experiments an average activity of 69 per cent (2,200 counts/min.) was detected. Thus, as in all previous groups observed, a substantial amount of the injected cardioplegic solution remained in the heart and was not associated with the return of normal rhythm. In this group only 1 animal failed to return to normal cardiac action before sacrifice. A residual activity of 65 per cent was observed in this dog.

A mean activity of 47,000 counts/gram/min. was demonstrated in the M_1 sample taken from all animals. From a knowledge of the weight of the heart, it may be estimated that approximately 90 per cent of the potassium injected is necessary to produce cardioplegia. This has been a constant finding. The activity of the second sample, M_2, taken at the termination of the experiment, was 21,000 counts/gram/min., or 44 per cent of the potassium injected to induce standstill.

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*Anton Electronic Laboratories, Inc., Brooklyn, N Y

With release of the aortic clamp there was a slow increase of radioactivity in the peripheral blood. Within 1 minute following the appearance of electrical activity on the cardiogram, every animal demonstrated an abrupt augmentation of K^{42} in the peripheral blood. When normal sinus rhythm resumed, a still further increase occurred for a short period, and then a steady decline was observed, so that, by termination of the experiment, 37 per cent of the activity detected in the first peripheral sample had disappeared.

The sample of coronary sinus blood taken after standstill was accomplished demonstrated an activity of 19,100 counts/ml./min. which represented 0.3 per cent of the amount of cardioplegic solution injected. This would indicate that during cardiotomy an insignificant amount of the injected potassium is aspirated by the coronary suction apparatus.

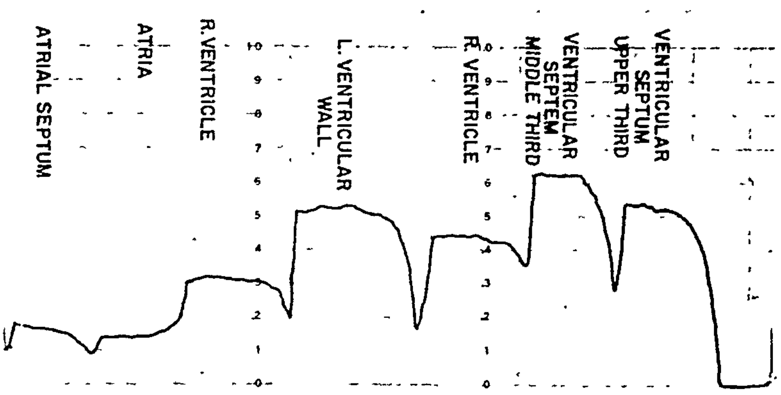

Fig. 2.—Residual K^{42} (counts/min.) in various areas of myocardium following cardioplegia and resuscitation using cardiac bypass.

The distribution of K^{42} detected in lung, kidney, and liver after sacrifice of animals was not uniform, there being 5,100, 2,900, and 800 counts/gram/min., respectively.

Measurement of radioactivity in various areas of the myocardium was carried out in vitro. A typical tracing is shown in Fig. 2. Average counts per minute of myocardium for all animals in this group were: left ventricle, 9,900; right ventricle, 8,800; atrium, 3,400; atrial septum, 4,200; upper third of the ventricular septum, 7,700; middle third, 11,100; and lower third, 8,700.

No change in blood pH was observed. Peripheral serum potassium averaged 3.7 before, 3.5 during, and 3.0 mEq./L. after cardiac bypass.

Hypothermia With Coronary Perfusion (GROUP II).—

An average of 13 ml. of potassium solution with a mean activity of 4.0 million counts per minute was necessary to produce cardioplegia in the 16 dogs of this group. A typical tracing demonstrating the changes in radioactivity of the heart during and after standstill and coronary perfusion is shown in Fig. 3. The pattern of activity observed is essentially similar to that reported for Group I, with one exception. Upon removal of the clamps in Group I, a gradual fall in radioactivity occurred, whereas, in this group, a more abrupt fall was observed. This may be attributed to cardiac massage expressing the potassium from the vascular compartment. Radioactivity remained fairly constant during the period of vascular occlusion and coronary perfusion. Coronary perfusion under the conditions of these experiments failed to effect a change in the concentration of potassium in the stopped heart, but, with removal of caval and aortic clamps, a drop in activity was observed. This decrease was continued with cardiac massage. As previously reported, both Figs. 1 and 3 demonstrate that the activity of the heart is independent of the concentration of potassium in the myocardium. From Fig. 3 it is observed that ventricular fibrillation, heart block, and sinus rhythm all occurred while the radioactivity remained constant.

During occlusion in the 16 dogs an average of 2,700 counts/min. was detected over the heart in situ. This was considered as 100 per cent of activity.

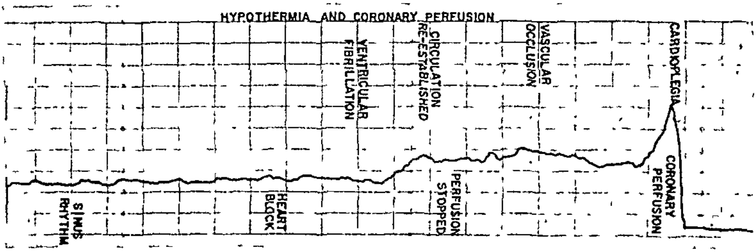

Fig. 3.—K^{42} (counts/min.) in the heart during and after cardioplegia with hypothermia and coronary perfusion. (Read from right to left.)

With cardiac massage, activity decreased to an average of 2,300 counts/min. (85 per cent of K^{42} injected). When cardiographic evidence of electrical activity was apparent, an average of 2,100 counts/min. (73 per cent of original activity) was present. This occurred at a mean time of 5 minutes after release of the occlusion clamps. At the termination of experiments, an average of 68 per cent of the original K^{42} (1,900 counts/min.) was obtained.

The first sample taken from the myocardium, M_1, which was considered representative of potassium incorporated during inflow occlusion, averaged 36,900 counts/gram/min. of heart muscle. The M_2 sample taken at the termination of the experiment averaged 13,500 counts/gram/min. of heart muscle. This represented 36 per cent of the activity incorporated into the myocardium at the time of occlusion. The apparent discrepancy between the activity detected at the end of the experiment by scanning over the heart (68 per cent of injected K^{42}) and counts obtained from the M_2 sample (36 per cent of potassium incorporated in the myocardium) is due to the fact that the former refers to radioactive counts per minute and the latter counts per gram per minute. Radioactivity was present, although not uniformly, in every organ assayed. At the termination of all experiments, specimens of lung contained an average of 5,900 counts/gram/min., kidney 2,500 counts/gram/min., and liver 1,697 counts/gram/min. Since no difference in activity of the various organs was observed in animals which had resumed normal rhythm and in those failing to do so, it is suggested that the cardiac massage was effective in re-establishing a fairly normal circulatory state.

The coronary sinus blood, including that coming from the coronary perfusion and the excess of the injected potassium solution, was collected and an aliquot was assayed for activity. An average of 15,800 counts/ml./min. was obtained. As in Group I, this represents 0.3 per cent of the injected cardioplegic agent.

As previously reported for hypothermic animals without coronary perfusion, an abrupt increase in K^{42} was detected in peripheral blood samples with removal of caval and aortic clamps. A peak of radioactivity occurred within 2 minutes after the onset of cardiac massage, and there was then a progressive gradual decline in the number of counts per sample. An average of 89 per cent of the K^{42} activity obtained in the first assay of peripheral blood had disappeared by the end of the experiments. No significant change in blood pH occurred at any time. With re-establishment of venous inflow, a slight elevation of serum potassium (7.0 mEq./L.) was encountered, but this promptly returned to the pre-occlusion level (5.0 mEq./L.). As evidenced by electrocardiographic tracings, 8 of the dogs returned to normal cardiac activity before termination of the experiments and sacrifice of the animals.

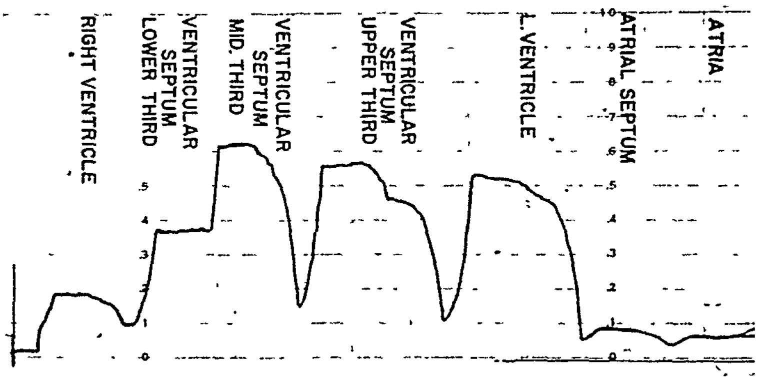

Fig 4.—Residual K^{42} (counts/min.) activity in various areas of myocardium following cardioplegia and resuscitation using hypothermia and coronary perfusion.

After sacrifice, the heart was removed. Atrial and ventricular myocardium and septum were separated and were individually assayed for radioactivity as in Group I. A typical tracing appears in Fig. 4. The average counts per minute for the 16 animals were 6,600 for the left ventricle, 2,400 for the right ventricle, and 900 for the atrium. The atrial septum yielded 1,200, the upper one third of the ventricular septum 7,500, the middle one third 8,700, and the lower one third 5,700 counts/min.

DISCUSSION

Previous studies by us demonstrated that when potassium was used as a cardioplegic agent in normothermic and hypothermic animals, reversibility to normal cardiac action was independent of the kinetics of this ion during resuscitation Observations recorded in this paper confirm our earlier findings, for total cardiac bypass and hypothermia with coronary perfusion during cardioplegia likewise failed to establish a relationship between the "washing out" of potassium and the recovery of cardiac function It would seem that potassium arrest has so altered the heart that merely removing occlusion clamps and permitting blood to flow through the coronary system is in most instances insufficient for a return to normal rhythm

The dynamic activity of the potassium ion and its intimate connection with cell membrane permeability must be considered It is well known that the concentration of potassium ion and its intracellular extracellular gradient plays an important role in the sequence of events related to electrical potential of the cell membrane This relationship between the extracellular potassium and the transmembrane potential has been expressed in terms of the mathematical equation $E = \log \frac{[Ki]^{*1}}{[Ko]}$ Thus, it may be seen how, by the injection of the cardioplegic solution (increasing Ko), this equilibrium might be altered That such an imbalance can be accomplished without damage seems extremely unlikely, for unless a normal equilibrium of potassium ion is rapidly re established on both sides of the cell membrane, and electric potentials reverted to normal, it is difficult to visualize a return to effective cardiac action

It has been demonstrated that the distribution of potassium between intracellular and extracellular fluids in living tissues is largely controlled by the cells themselves Yet, this factor of self regulation is probably dependent upon a normal cardiac action, for it has been demonstrated in these experiments that it was such an action—and not the mere mechanical work of the pump—which was effective in eliminating potassium from the myocardium While there was an increase of K^{42} in peripheral blood immediately upon release of occlusion clamps, in every experiment there was a further increase with the onset of some kind of cardiac activity This increase was further augmented subsequent to the resumption of a normal sinus rhythm To break this cycle, that is, the interdependence of myocardial cell function and normal cardiac activity, in our experience maintenance of good coronary circulation has been considered to be mandatory

Because Effler and colleagues[6] have stated that a high speed coronary flow will aid the heart in its recovery from cardioplegia, in several experiments following removal of occlusion clamps we increased the flow from 65 ml /kg /min to 100 ml /kg /min No difference in the speed of recovery or in the presence of arrhythmias was observed While such perfusion might be expected to eliminate potassium in the vascular space, intracellular potassium cannot be eliminated by such mechanical means, for had such measures been effective, animals in Group II (coronary perfusion) might have been expected to demonstrate a greater amount of K^{42} in the atrial blood sample and a lesser activity in the M_1 myocardial sample

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*E = electropotential difference Ki = intracellular potassium Ko = extracellular potassium

In these experiments a cardioplegic threshold was reached when an average of 40,000 counts of K^{42} was incorporated into each gram of myocardium. A greater amount of potassium is required to approach the cardioplegic threshold in clinical open heart surgery when long-standing disease has caused dilatation of the chambers and hypertrophy of the myocardium to three or four times the normal size. Since 44 per cent of the injected potassium in Group I and 36 per cent in Group II were found in the myocardium at the end of these experiments, it might well be expected that the amount of residual potassium in clinical cases will likewise be of larger magnitude.

Our studies have indicated that the remaining cardioplegic agent (potassium) cannot be indicated as the factor responsible for the production of temporary arrythmias, bundle branch block, fibrillation, etc. It is our impression that perhaps the only part of the procedure of induced standstill which is entirely a function of the amount of potassium injected is the cardioplegia itself. Events following the inception of standstill are influenced by factors which at present are unknown.

Elective cardiac arrest is often followed by cardiac arrhythmias. In Group I only 2 animals fibrillated, whereas, in Group II (coronary perfusion and hypothermia) 90 per cent of the dogs fibrillated one or more times after the reestablishment of the coronary flow. Electric shock was used for defibrillation. The 2 animals of Group I reverted to sinus rhythm immediately after defibrillation, whereas in Group II only 50 per cent reverted to sinus rhythm after demonstrating a variety of arrhythmias, the most common of which was heart time during resuscitation. Effler and colleagues[2] have reported that in several block. Thirty per cent of the dogs in Group I demonstrated heart block at some cases complete heart block has occurred when anatomic disruption of the conduction bundle seemed unlikely, and they attributed this to poor perfusion of the myocardium and surgical trauma. Melrose,[8] in discussing the same paper, stated that " . . . hearts will always start again provided they are not overstretched." In our experiments, surgical trauma was slight since little was done to the heart itself, coronary perfusion was satisfactory, overstretching of the myocardial fibers was avoided, and there was no anatomic disruption of the conduction system, since stitches were not placed near the septum. In spite of this, arrhythmias were not avoided during the period of resuscitation.

To evaluate the possible role of potassium as an etiologic factor producing these disturbances, the amount of this ion accumulated in various areas of the heart was determined. More K^{42} was found in the atrial septum than in the atrial myocardium; more in the ventricular septum than in the ventricular muscle; and a greater amount in the left than in the right ventricular wall. The greatest radioactivity was registered in the middle one third of the ventricular septum. Perhaps these differences may be due to a greater vascularity and larger muscle mass in the ventricular septum. Whatever the explanation, it would seem that frequent and persistent arrhythmias might be due to the greater amount of potassium accumulated in the path of the conducting system.

SUMMARY

Potassium is being used clinically as a cardioplegic agent in spite of limited physiologic knowledge concerning the fate of this ion. Previous studies by us in normothermic and hypothermic animals demonstrated that (a) reversibility of cardioplegia was not uniformly related to the amount of potassium injected or to its myocardial concentration, and (b) that "washing out" potassium did not imply a resumption of normal rhythm.

In this investigation, information was obtained concerning the fate of potassium (K^{42}) used as a cardioplegic agent in animals subjected to either total cardiac bypass or hypothermia with coronary perfusion. These studies, aside from adding confirmation to our previous findings, supply evidence that (1) once potassium induced cardioplegia is accomplished, its reversibility is largely beyond our control; (2) mechanical means are effective in "washing out" only the potassium accumulated in the vascular space and that re-establishment of normal intra- and extracellular equilibrium of this ion is dependent upon other factors; (3) there is an uneven distribution of potassium (K^{42}) within the heart, the greatest amount found in the middle one third of the ventricular septum, which might explain the frequent and persistent arrythmias which occur following the use of this agent; and (4) experimental data suggest that the indiscriminate use of potassium as a cardioplegic agent is hazardous.

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POSTOPERATIVE EAR OXIMETER STUDIES IN THORACOTOMY PATIENTS

II. Variations With Operative Procedures and With the Stir-up Regime

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INVESTIGATION of pulmonary physiology in post-thoracotomy patients has largely been concerned with the late results of resectional surgery or thoracoplasty. There are few reports of such studies in the immediate postoperative period. Hood and Beall[1] demonstrated arterial oxygen desaturation and respiratory acidosis developing in about 50 per cent of patients in the first hour after anesthesia. Alveolar hypoventilation was considered the major functional derangement. Mastio and Allbritten[2] extended such studies to the first postoperative day. They found that alveolar hypoventilation continued through the first postoperative day, and that both respiratory and metabolic acidosis developed following eight upper abdominal operations, and seven nonresective thoracic operations. Blair and Hickam,[3] in their study of intrapulmonary gas mixing, included data on lung volumes, minute ventilation, and maximum breathing capacity in the second week postoperatively in 5 lobectomy patients. They found normal ventilation by this time, but demonstrated increased impairment in intrapulmonary gas mixing. Our group recently made a preliminary report on arterial blood oxygen saturation for 10 consecutive postoperative days on patients undergoing pulmonary resections.[4] Saturations were found to be lowest on the second and third postoperative days. Extension of these studies should provide a more rational approach to the care of postoperative patients. To this end we have begun investigation of various parameters of pulmonary function. The purpose of this report is threefold: (1) to present in detail the daily oxygen saturation in patients undergoing various procedures, (2) to corroborate the value of the stir-up regime, and (3) to present certain arguments bearing on the mechanism of postoperative arterial blood oxygen desaturation.

METHODS AND MATERIAL

Sixty-two male patients undergoing 63 thoracic operations for tuberculosis were studied. Arterial blood oxygen saturation was determined, using a single

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scale ear oximeter. The same ear piece was used throughout the stu
same two anesthesiologists performed the tests. The ear piece was al
warm the pinna of the ear until a constant reading was established, usually 5 to 10 minutes. The preoperative arterial blood oxygen saturation was determined either the day before the operation, or on the morning of the operation after the administration of only a belladonna alkaloid as preanesthetic medication. Postoperative determinations were made on the operative day and for 10 consecutive postoperative days. After the saturation at rest was recorded the patient was asked to take 3 or 4 deep breaths. A second reading was recorded when the galvanometer restabilized.

Twenty-six patients had operations consisting of resection of one or two segments of the lung. The raw surfaces of the remaining segments were covered with pleura as much as possible to decrease air leak. Two of this group had postoperative atelectasis, 1 requiring bronchoscopy. Two others had hemorrhage requiring re-operation. Saturations for the latter were recorded as days after the second operation. Only 3 patients received oxygen therapy longer than 24 hours, and none longer than 48 hours postoperatively. Narcotics were used discriminately to relieve pain and the stir-up regime was mandatory.

Twenty-three patients underwent excision of a pulmonary lobe. Six of this group had atelectasis, 2 requiring bronchoscopies. One additional patient had atelectasis and pneumonitis requiring continued oxygen therapy. He died of respiratory insufficiency on the tenth postoperative day. No other patient required oxygen therapy beyond 36 hours. Narcotic administration and nursing care were comparable to the first group.

Thirteen patients underwent more extensive procedures, including pneumonectomy, thoracoplasty, extensive decortication, and plombage. These patients were grouped together as miscellaneous procedures, both out of statistical necessity, and because it was thought there was a greater compromise of lung tissue than with the previous two groups. There was one death, 2 days postpneumonectomy, and 2 cases of atelectasis not requiring bronchoscopy. No patient required oxygen after 36 hours, except 1 who was moribund. In this group, also, narcotic administrations were individualized and frequent stir-ups demanded.

RESULTS

The daily saturations and standard deviations of each of the three groups and of the entire group are presented in Table I. The distribution of individual saturations within each group was far from the "normal curve," being skewed with the tail toward desaturation. The standard deviations quoted are therefore large, but do provide an estimate of the range of the individual saturations. The highest saturations were recorded on the operative day in all three groups. This is a reflection of the routine administration of oxygen therapy on this day. Oxygen saturations decreased for 48 hours. Thereafter the average saturation for the lobectomy and segmental resection group tended to rise slowly toward normal at the end of a week. Patients undergoing more severe operations had lower saturations and did not attain preoperative levels within the first 10 days of the study. There was a tendency observed with the lobectomy patients to have a slightly higher saturation on any given day than those patients undergoing segmental resections. The higher preoperative and operative day averages of the lobectomy group suggest that this may be due in part to a systematic error in the measurements. However, the greater variance of the segmentectomy group support a conclusion of greater disability for many patients in this group.

TABLE I. DAILY ARTERIAL OXYGEN SATURATION

OPERATION	PREOP.	DAY OF OPERATION	POSTOPERATIVE DAY									
			1	2	3	4	5	6	7	8	9	10
23 Lobectomy												
Average saturation	94.8	97.2	92.6	90.5	92.8	93.5	91.6	93.4	93.5	95.0	94.6	93.2
± S. D.	3.3	3.0	4.9	5.8	3.8	3.0	3.8	3.4	5.0	2.7	3.6	4.1
26 Segmental resection												
Average saturation	92.8	95.8	92.1	89.2	91.1	91.3	92.6	91.4	92.7	93.3	94.0	94.0
± S. D.	5.58	3.75	4.8	5.8	5.7	5.3	4.8	4.4	3.4	3.4	4.0	2.5
14 Miscellaneous												
Average saturation	92.5	95.8	92.8	87.4	88.7	92.2	89.8	90.1	91.3	90.7	89.6	90.5
± S. D.	4.4	3.6	4.0	9.6	7.2	3.5	5.9	5.6	6.3	3.5	8.0	6.4
Average of 63 operations												
Average saturation	93.5	96.2	92.5	89.3	91.2	92.4	91.6	91.9	92.8	93.5	93.4	93.0
± S. D.	4.8	5.9	4.7	6.9	5.5	4.3	4.9	4.3	4.7	3.7	5.1	4.4

TABLE II. CHANGE IN SATURATION WITH 3 TO 4 DEEP BREATHS

OPERATION	PREOP.	POSTOPERATIVE DAY									
		1	2	3	4	5	6	7	8	9	10
Lobectomy											
On air	94.8	92.2	90.9	92.7	93.6	91.5	93.4	93.5	95.0	94.6	93.2
After 3 to 4 deep breaths		96.3	94.8	95.4	95.8	95.1	96.0	96.0	96.4	96.4	95.1
Rise in saturation*		4.1	3.9	2.7	2.2	3.6	2.6	2.5	1.4	1.8	1.9
Segmental resection											
On air	93.7	91.2	89.2	91.1	91.2	92.6	91.4	92.7	93.3	94.0	94.0
After 3 to 4 deep breaths		95.0	94.1	94.5	93.1	95.6	94.0	95.5	95.8	96.1	95.7
Rise in saturation*		3.8	4.9	3.4	1.9	3.0	2.6	2.8	2.5	2.1	1.7
Miscellaneous											
On air	93.7	91.5	87.2	88.7	92.2	89.8	90.1	91.3	90.7	89.6	90.6
After 3 to 4 deep breaths		94.4	91.9	92.9	94.8	93.5	93.6	95.0	94.4	93.1	93.2
Rise in saturation*		2.9	4.7	4.2	2.6	3.7	3.5	3.7	3.7	3.5	2.6

*Significant at the 1 per cent level in all days and all groups.

There was a greater tendency for the segmental resection patients to exhibit higher saturations than the miscellaneous group. These observations were obscured somewhat by the wide scatter of the saturations in each group, but when the entire postoperative period is examined, the difference between lobectomy and segmentectomy patients, and between segmentectomy and miscellaneous procedures is significant (P less than 0.02 per cent).

Table II presents the change in saturation measured after 3 or 4
Only patient days without oxygen therapy were included in this con
P values were calculated by Student "t" test The rise in saturat
these few deep breaths is striking and highly significant (P less tha
The increase was in part dependent on the degree of resting desaturati
greatest increase was on the second and third postoperative day whe
tions were lowest, averaging 3 9 to 4 9 per cent increase All thre
showed comparable increases

Ten patients had clinical and/or roentgen signs of atelectasis on which the patients underwent bronchoscopies or on which they were given a "tracheobronchial toilet" or other definitive therapy, was designated as a "critical day" Table III presents the average oxygen saturations of these patients on the critical day and for 2 days before and after The change in saturation from the day before to the day after the critical day is significant (P less than 0 05 per cent) even for this small group of patients

TABLE III SATURATIONS OF 10 PATIENTS WITH ATELECTASIS

	2 DAYS BEFORE CRITICAL DAY	1 DAY BEFORE CRITICAL DAY	CRITICAL DAY	1 DAY AFTER CRITICAL DAY	2 DAYS AFTER CRITICAL DAY
Resting saturation ± S E	90 1 1 3	88 9 1 7	90 0 1 6	93 7 1 2	93 4 1 5
After stir up ± S E	93 1 3 7	92 0 2 1	93 4 1 7	96 0 1 3	95 9 0 7

DISCUSSION

There is a certain amount of stimulation and anxiety on the part of the patient which attends arterial puncture which would tend to mask hypoxemia if it were due to hypoventilation The value of the single scale oximeter in estimating arterial blood oxygen saturations has been widely questioned However, we feel that when it is used to compare day-to day or minute to minute changes in the same patient, it is a clinically useful tool Further, when large numbers of estimations are statistically grouped, the relative changes are thought to be quite reliable

An average decrease in saturation could be produced by a few very desaturated patients This was not the case in our patients Fig 1 shows the frequency distribution of saturations for the entire series over the 12 day period studied It demonstrates that modal and median saturations are depressed in the first 72 hours postoperatively, and rise slowly in the next 7 days

The desaturation described in our initial report might have been due to a disproportional desaturation attending a specific operative procedure That this was not true is most clearly shown in Fig 2 Although there is some difference between the values of each of the three operative groups the similarity of the shapes of the graphs is striking One would expect the technique of segmental resection to produce a greater although temporary alteration in pulmonary function than the procedure of lobectomy. Our results substantiate such a view and are consistent with the anticipation of greater alterations in physiology following pneumonectomy, decortication, thoracoplasty, etc.

It is commonly observed that patients who seem to be doing well on the operative afternoon or on the first postoperative day may later develop pulmonary complications. This suggests there are progressive changes continuing for several days. The finding of lower saturation on the second and third days than on the operative or first postoperative day is evidence for such continuing changes. To be sure, many patients developed minimal desaturation in the first several days, but many others had marked desaturation. Clinically evident cyanosis was uncommon except in the very ill. Desaturation on the second or third day was not predictive of subsequent complications or prolonged morbidity. Some patients with saturations in the range of 85 to 90 per cent did not have clinically evident complications But certainly any patient with decreased arterial oxygen content runs a greater risk of complication.

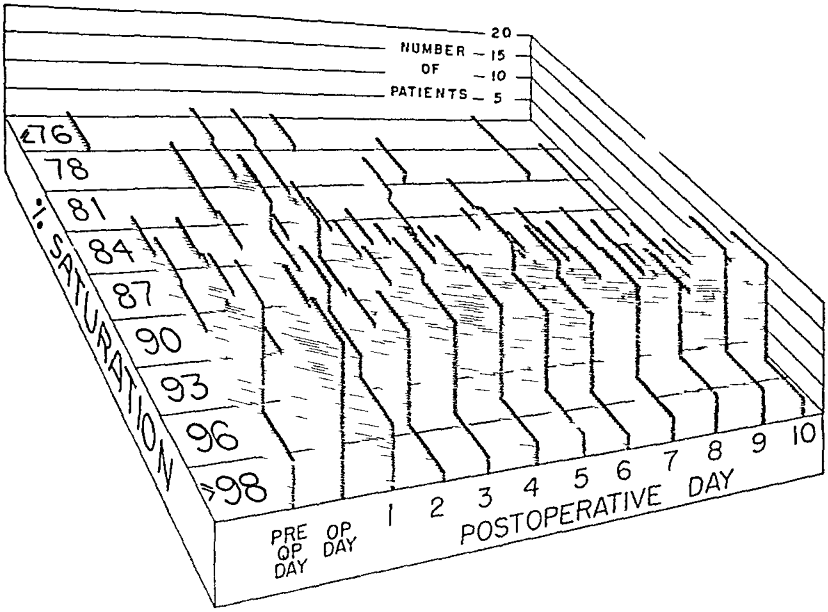

Fig 1 —Three-dimensional histogram of the day-to-day saturations One the horizontal axis extending back into the distance the saturations have been pooled into groups of 3 per cent The heights of the histograms represent the number of patients with saturations in the indicated 3 per cent interval The skewed distribution of the values is evident This diagram demonstrates that the trend to desaturation is a general one, although there may be considerable difference in degree of desaturation from patient to patient

There are three points that can be made from these data. (1) More extensive surgery seems to produce more extensive alteration in function. (2) Therapy directed specifically toward pulmonary complications is effective. This is demonstrated both by the increase in oxygen saturation following 2 or 3 deep breaths, and by the increase in saturation in those patients with atelectasis, following bronchoscopy, tracheobronchial toilet, etc. (3) Whatever alteration in function may be responsible for the desaturation, it is in large part reversed by a few voluntary deep breaths Inspection of Fig 3 shows an almost saturation reached after 3 or 4 deep breaths, no matter what day or resting saturation might be

At our altitude, normal alveolar pO_2 is approximately 100 to 110 This cannot be increased except by oxygen therapy or by hyperventilation sufficient and prolonged enough to lower significantly the alveolar pCO_2 Even if

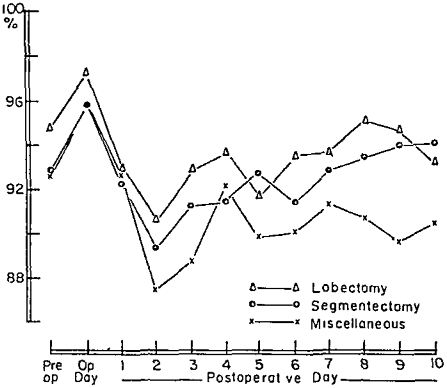

Fig 2 —Average saturations in three groups of patients undergoing open thoracotomy

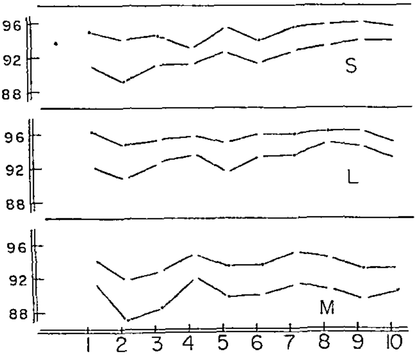

Fig 3 —Comparison of average saturations in three groups of patients before and after 3 or 4 deep breaths No patient receiving oxygen was included in this compilation The preoperative average saturation is represented by a dot at the left of each pair of graphs The groups are identified by *L*—lobectomy *S*—segmental resection *M*—miscellaneous procedures

the deep breathing utilized in this experiment were sufficient to lower the pCO_2, it would have returned toward the initial level by the time the oximeter was recalibrated Therefore, the rise in saturation must be due in greatest part to a mechanism which does not involve a supranormal alveolar pO_2

Diffuse subclinical atelectasis has been suggested as a possible mechanism of arterial desaturation in postoperative patients. One would not expect 3 or 4 deep breaths to re-expand large portions of such atelectatic areas. Nor would elevation of alveolar pO_2 with oxygen therapy in such circumstances result in significant elevation of arterial blood oxygen saturation. Thus, the marked increase noted on the operative day is inconsistent with diffuse collapse at that time. In 10 patients with definite atelectasis, specific therapy directed toward the complication was found to increase the saturation significantly. An increase in saturation with deep breathing was noted both before and after resolution of the atelectasis. This indicates that there were additional mechanisms for desaturation.

Reduction in diffusion capacity of the lung for oxygen has also been suggested as another mechanism for desaturation.[4] The normal diffusing capacity for oxygen is approximately 20 to 25 c.c. O_2/minute/mm. Hg/$M.^2$ body surface. It would require a reduction of 75 per cent to produce the observed saturations in the average patient, i.e., an increase in driving pressure gradient of oxygen of 400 per cent. From the flattening of the oxygen-hemoglobin dissociation curve above 90 per cent saturation, one must conclude that a rise in arterial saturation of the magnitude observed after deep breathing would be possible only with a supranormal alveolar pO_2, if a diffusion defect were the primary mechanism involved. If there were a diffusion defect in these patients, it was neither very great nor responsible for the observed desaturation.

Possible mechanisms for arterial desaturation include alveolar hypoventilation with either depression of the central nervous system or mechanical impairment including pain, defects in intrapulmonary gas mixing, or alteration in the ventilation-perfusion ratio. Hypoventilation has been documented in the first 24 to 36 hours postoperatively[1, 2] and is the most probable cause of prolonged desaturation. More specific pulmonary function testing may confirm this view and indicate the relative importance of depression, pain, and mechanics.

SUMMARY

The day-to-day oxygen saturations in 63 open thoracotomy cases are presented. The three surgical groups, lobectomy, segmental resection, and miscellaneous procedures, were shown to be qualitatively similar with greatest desaturation in the second postoperative day and improvement slowly thereafter. Quantitatively, the miscellaneous group exhibited the greatest desaturation and the lobectomy group the least, but the segmentectomy group had the most rapid recovery. Saturations in all three groups after a few deep breaths were found to approach normal. This excludes diffuse subclinical atelectasis and defects in diffusion in the lung as likely mechanisms producing the arterial saturations observed.

Appreciation is expressed for the help of Paul E. Sadler, M.D., for assistance in the early portion of this work, and to Richard H. Wasserburger, M.D., for assistance in preparation of the manuscript.

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TECHNICAL PROBLEMS IN THE SURGICAL REPAIR OF INTRATHORACIC ANEURYSMS

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The major problems associated with the surgical management of thoracic aortic aneurysms are concerned either with vascular occlusion required during the course of the repair or with technical aspects of the actual repair. Whether or not complete vascular occlusion is required depends upon both the type of aneurysm present and the kind of repair utilized. For example, a saccular aneurysm in which the neck can be isolated, clamped, and sutured will not necessitate complete occlusion of the aorta, while a fusiform or large saccular one which is to be completely excised and replaced with a suitable graft will require complete proximal and distal occlusion.

The ill effects of cross-clamping the aorta arise from the increased pressure which results proximal to the occlusion and/or from the decreased pressure and resultant decreased blood flow distal to the occlusion. The degree of hypertension which occurs proximal to the occlusion depends upon the level of the occlusion. Cross-clamping the arch of the aorta produces a greater increase in proximal pressure than clamping the aorta just above the diaphragm. The more proximal cross-clampings may produce such a high pressure and increased resistance that acute heart failure or cerebrovascular accident may be precipitated.

Of more common occurrence are the results of decreased blood flow distal to the occluded segment. The tissues of the central nervous system are most sensitive to ischemia. Occlusion proximal to the left common carotid artery may produce hemiplegia, although not infrequently good blood flow through one common carotid artery may be sufficient to nourish the entire brain. One of the greatest hazards of thoracic aortic occlusion is the risk of spinal cord ischemia, since the chief components of the anterior spinal artery are composed of the radicular branches from the thoracic aorta.[1]

Clinical experiences with the length of time during which the descending thoracic aorta may be safely occluded have varied. Crafoord[2] successfully occluded the aorta for 27 minutes while repairing a patent ductus arteriosus, while Chamberlain[3] stated that neurologic damage may follow occlusion for 24 minutes. Adams[1] recently gave 18 minutes as probably the maximum safe occlusion time. In our own experience, paraplegia resulted from a 13-minute

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occlusion associated with the insertion of a Hufnagel valve, although in this instance ligation of three pairs of intercostal arteries may have contributed to the spinal cord ischemia.

Since other tissues are normally much less sensitive to hypoxia than nervous tissue, measures taken to avoid cord damage usually are adequate to protect the kidneys and other tissues within the abdomen.

One very serious hazard which is probably the result of peripheral hypoxia is the diminished peripheral resistance which not infrequently follows periods of aortic occlusion. Severe hypotension may occur as the occluding clamp is released, in spite of releasing the clamp slowly and in spite of adequate blood replacement and/or vasopressor agents

Surgical exposure must be wide enough to allow an approach to the aorta at a safe distance from the aneurysm, both proximally and distally. The aorta should be exposed on each side of the aneurysm prior to dissection near it since, if the aneurysm is inadvertently entered, prompt control is mandatory.[4] We have favored bilateral anterior thoracotomy with median sternotomy for aneurysms of the ascending aorta or arch, although other approaches may be used[5] Closure of the wounds has not been a problem and disruption has occurred in only one instance, following extensive mediastinitis

The following case histories, most with an unfavorable outcome, have been selected from our experiences to illustrate some of the more common problems which arise in management of the various types of thoracic aneurysms

CASE REPORTS

A *Aneurysm of Ascending Aorta.*—

CASE 1 —J. G , a 44 year old Negro man, had an orange sized syphilitic aneurysm arising from the ascending aorta and projecting anterolaterally to the right (Fig. 1, *A*). Exposure was obtained through a right anterior thoracotomy in the third intercostal space with median sternotomy to the jugular notch. The aneurysmal neck was occluded easily with a cloth covered intestinal clamp, enabling excision and repair with interrupted No 3 0 silk sutures (Fig. 1, *B*). The ascending aorta was thus reconstructed to a normal diameter.

CASE 2 —J C, a 45 year old white man, had a syphilitic aneurysm involving the left aspect of the ascending aorta and inferior aspect of the arch (Fig 2, *A* and *B*). The large, grapefruit sized aneurysm was quite adherent to the trachea posteriorly and pulmonary artery anteriorly Anatomically, this sac was so situated and its neck was so wide that it could not have been managed by means of a lateral reconstruction without aortic occlusion It was planned to use a temporary shunt enabling aortic occlusion with reconstruction of the arch, however, the sac was inadvertently entered at the junction of the sac and ascending aorta Massive bleeding which followed was controlled by placing a clamp parallel to the ascending aorta on the neck of the aneurysm and across the aortic arch distal to the innominate artery. Cardiac arrest occurred but with rapid blood replacement and cardiac massage an effective heartbeat was restored With the arch occluded and blood flowing to the brain through the right innominate artery, the inferior aspect of the arch was reconstructed (Fig 2. *C*) Although the patient survived the surgery, he died later from cerebral damage

The successful management of this type of aneurysm necessitates measures to avoid cerebral ischemia In 1 patient, operated upon with Dr. Mark Wolcott at the Veterans Administration Hospital, the innominate and left common carotid arteries were occluded 15 minutes during a restorative endoaneurysmorrhaphy. Blood flow to the brain was thus limited to the left vertebral artery during the repair. The patient survived without evidence of neurologic damage only to die later of other complications.

Hypothermia of a moderate degree (lower limit, 90° F.) adds considerable protection to the brain in aneurysms in this area. When the aneurysm is in the innominate artery and temporary occlusion of the left common carotid is necessary, hypothermia may be adequate to protect the brain.

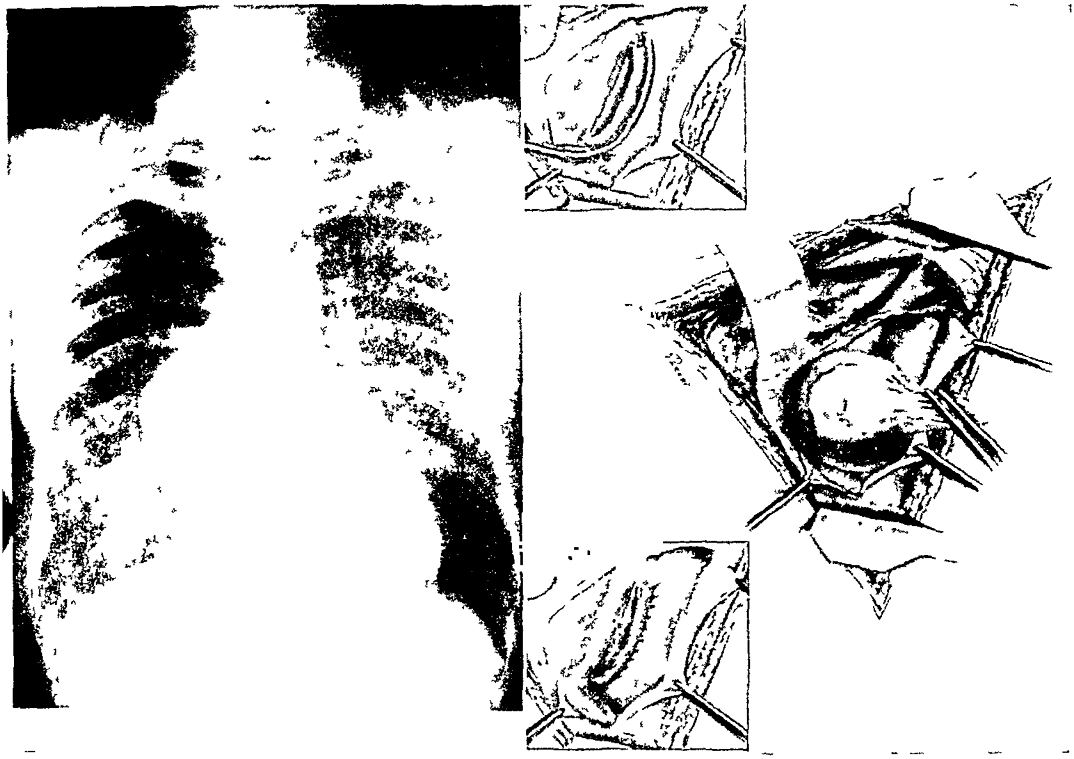
A B

Fig. 1—*A*, Posteroanterior x-ray of chest showing saccular aneurysm of ascending aorta *B*, Lateral aortorrhaphy.

On the other hand when an aneurysm is as extensive as in Case 2, arch replacement probably should be the goal. This would necessitate a bypass shunt from ascending aorta to cerebral vessels and distal aorta Considerable experimental and clinical studies have been presented by Izant,[6] Hardin,[7, 8] Stranahan,[9] Cooley,[10] and Creech[11] and their associates. The shunts must be of sufficient inside diameter to avoid increased resistance to flow, otherwise acute left heart failure may occur. Hardin and associates[8] demonstrated experimentally that the heart would not tolerate shunts of small diameter and that hypothermia and partial inflow stasis were necessary if small shunts were used. Stranahan[9] suggested shunts with an inside diameter of 10 mm. or larger in the presence of hypertension or coronary disease. During arch replacement, Cooley and associates[10] combined hypothermia and a shunt with an inside

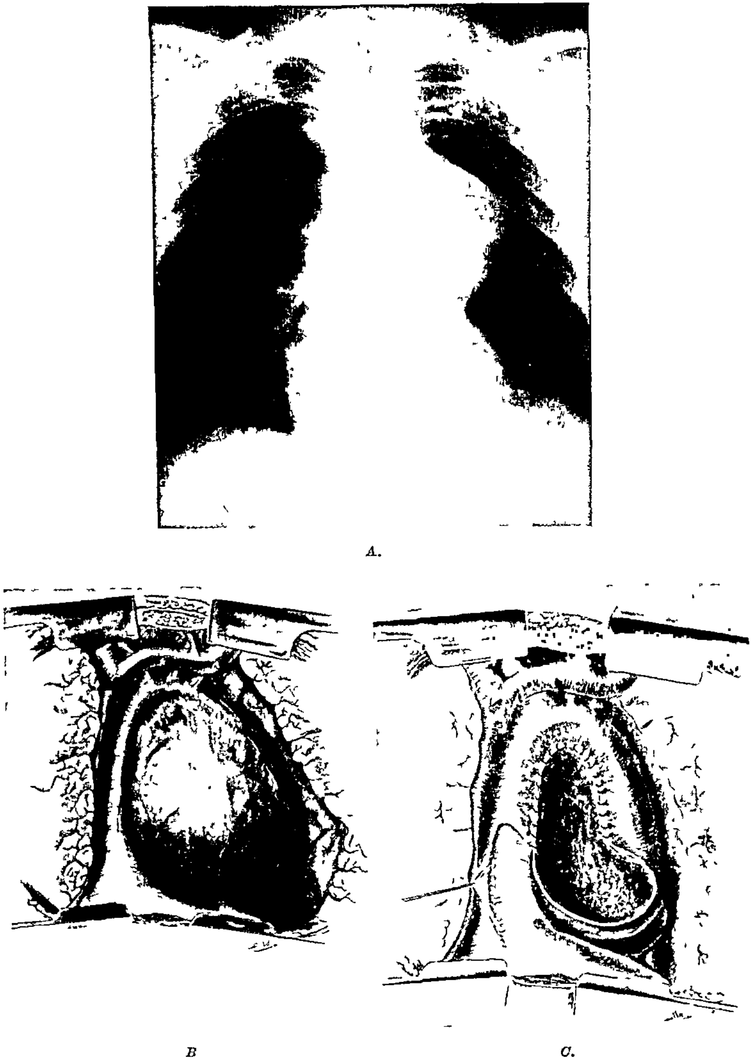

Fig 2 —*A*, Posteroanterior x-ray of chest which shows large aneurysm arising from inferior aspect of aortic arch *B*, Drawing which shows large aneurysm arising from inferior aspect of aortic arch *C*, Drawing which shows completed reconstructive aneurysmorrhaphy

diameter of 14 mm. with fall in pressure distally of only 10 mm. Hg when the aorta was occluded. Without the use of hypothermia, larger shunts, probably up to 2 cm. in diameter, will be necessary.[11]

Recently De Bakey and associates[12, 13, 14] have presented another approach to aortic aneurysms. During total cardiac bypass, using a modified DeWall-Lillehei pump-oxygenator, aneurysms of the ascending aorta and arch have been successfully operated upon.

B. *Aneurysms of Innominate Artery and Arch of Aorta.*—

Aneurysms involving the innominate artery frequently can be satisfactorily managed by means of aneurysmectomy with ligation of the right subclavian and common carotid arteries. More often, however, there is associated involvement of the aortic arch or the aneurysm arises in the innominate adjacent to the arch so that there is a wide neck of several centimeters at the arch. In this area, aneurysms are densely adherent to the superior vena cava, innominate vein, and trachea, and frequently have eroded into the anterior chest wall. Such an aneurysm must be approached widely and extreme precautions are necessary in its mobilization until the proper time arrives to occlude its neck.[4] If the left common carotid artery is not involved it is usually densely adherent to the wall of the aneurysm and must be separated with care.

CASE 3.—J. J., a 65-year-old Negro man, had a saccular aneurysm of the innominate artery which filled the superior mediastinum and presented in the low anterior cervical region as a large orange-sized pulsating mass (Fig. 3, *A* and *B*). This aneurysm was approached through an anterior bilateral thoracotomy in the third intercostal space combined with median sternotomy to the jugular notch. Since it was necessary to occlude the left common carotid artery when the neck of the sac was occluded, a compressed Ivalon sponge graft* was placed from the side of the ascending aorta to the end of the divided right common carotid (Fig. 3, *C*). Cerebral blood flow was maintained through the left carotid for 50 minutes while the graft was placed on the right. Thereafter, cerebral flow was provided through the graft to the right common carotid for 40 minutes while the aneurysm was being removed. All of the aneurysm was removed except its posterior wall which was densely adherent to superior vena cava, trachea, and mediastinal tissues. Postoperatively, the patient developed an extensive mediastinitis which could have been related to the residual sac or the plastic prosthesis. Even though he had cerebral flow through one carotid artery at all times and eventually in both, right hemiparesis developed. This was improving when he began to deteriorate from mediastinal infection. His death resulted from exsanguination due to rupture of the aorta adjacent to the suture line at the base of the left common carotid artery.

It has been demonstrated by Bahnson[4] that sacrifice of the innominate artery is tolerated unusually well; in one paper he mentions that this had been done in 5 patients without sequelae. There is an approximate mortality of only 5 per cent with ligation of one carotid artery but a morbidity as high as 40 per cent.[15]

CASE 4.—T. B., a 50-year-old Negro man, had a very large innominate artery aneurysm which proximally involved the aortic arch and distally extended well into the neck (Fig. 4, *A*). The aneurysm was exposed through an anterior bilateral thoracotomy in the fourth intercostal space. It seemed to arise from the arch with a base of some 5 cm. Prior to dissecting around the aneurysm, a 2 cm. diameter temporary bypass shunt of compressed Ivalon sponge was sutured to the side of ascending aorta and descending aorta beyond the arch. About the midpoint of the Ivalon shunt was a T-limb into which was inserted a plastic Y adapter

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*The use of compressed Ivalon sponge grafts has been discontinued.

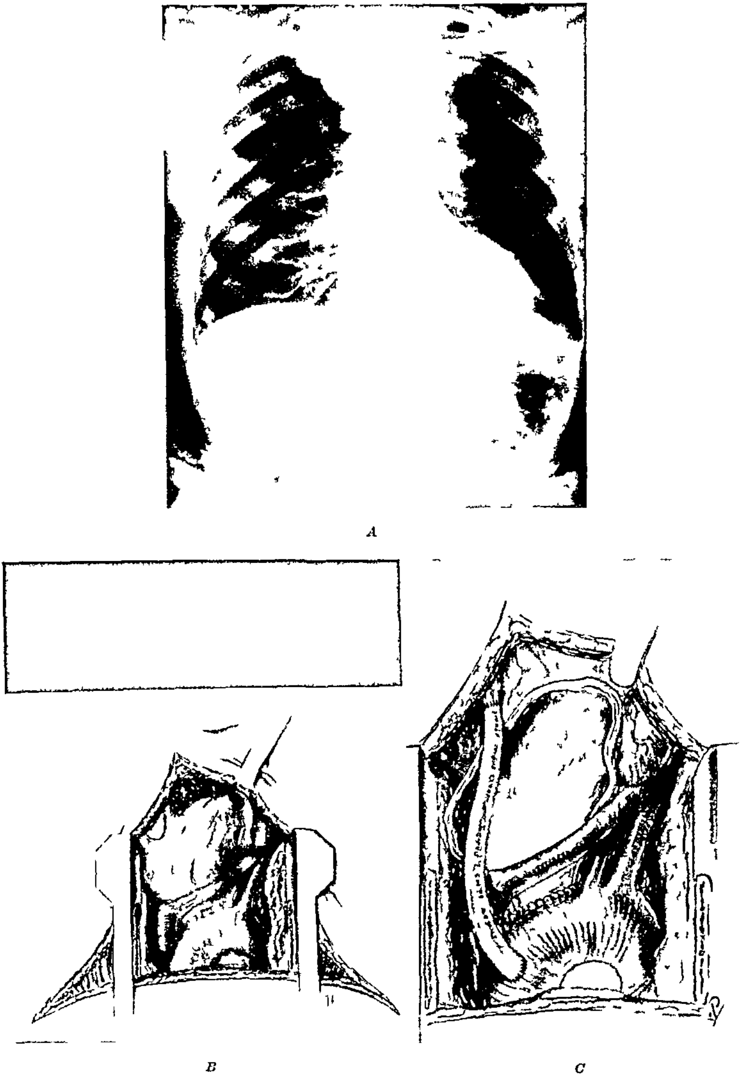
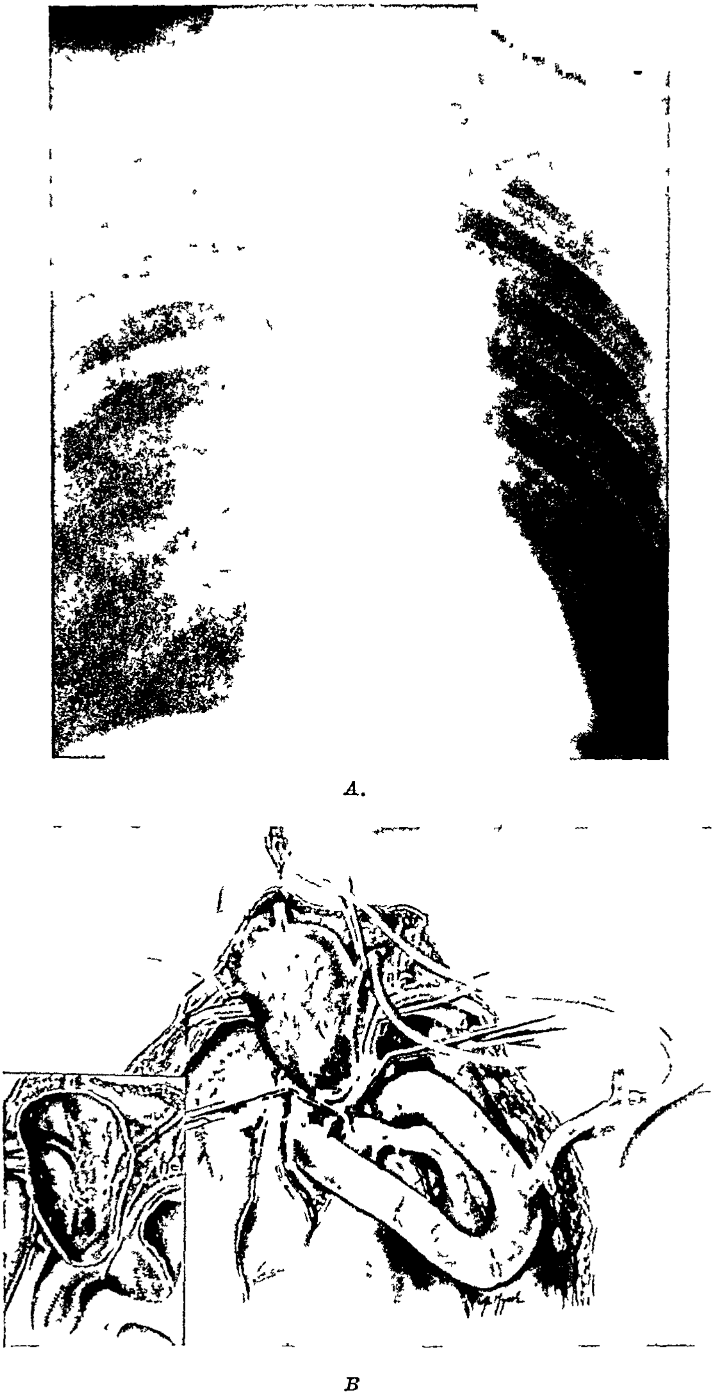


Fig 3.—*A* Posteroanterior x ray of chest which shows large aneurysm arising in innominate artery at its origin from the aortic arch *B*, Drawing which shows large aneurysm arising in innominate artery at its origin from the aortic arch *C* Drawing which shows completed repair with compressed Ivalon graft from aortic arch to innominate artery

with two No. 16 F. plastic catheters which were inserted into the carotid arteries, the right in the neck and the left within the thorax (Fig. 4, *B*). The arch was then isolated by occlusive clamps while circulation was maintained to all organs through the shunt. The femoral artery pressure, which was being monitored with a Statham transducer and Cambridge recorder, did not change with aortic occlusion and remained at about 100 mm. Hg systolic during the hour on the bypass. Cardiac function seemed good during the bypass, indicating



A.

B

Fig 4.—*A*, Posteroanterior x-ray of chest which shows innominate artery aneurysm extending into neck. *B*, Drawing which shows temporary bypass graft to provide blood flow to brain and distal organs during reconstruction of aorta.

that the size of the shunt was adequate After aortic occlusion, the aneurysm w
widely and evacuated of thrombus in varying stages of organization. The ne
aneurysm was found to be 5 cm in length, arising at the junction of the arch, i
artery, and left common carotid arteries Reconstruction was accomplished with c
sutures of No. 2 0 silk in such a manner as to restore flow through all head arteries
the sac wall was excised, but it did not seem feasible to attempt excision of the sa
adherence to trachea, superior vena cava, and innominate artery. The bypass funct
and technically the repair was satisfactory During the latter part of the operati
from all raw surfaces became quite severe, although bleeding had not been a proble
The patient failed to respond to the usual measures and died in the recovery roo
hours postoperatively while receiving the twenty fifth pint of blood

C. *Aneurysms of Descending Thoracic Aorta*—

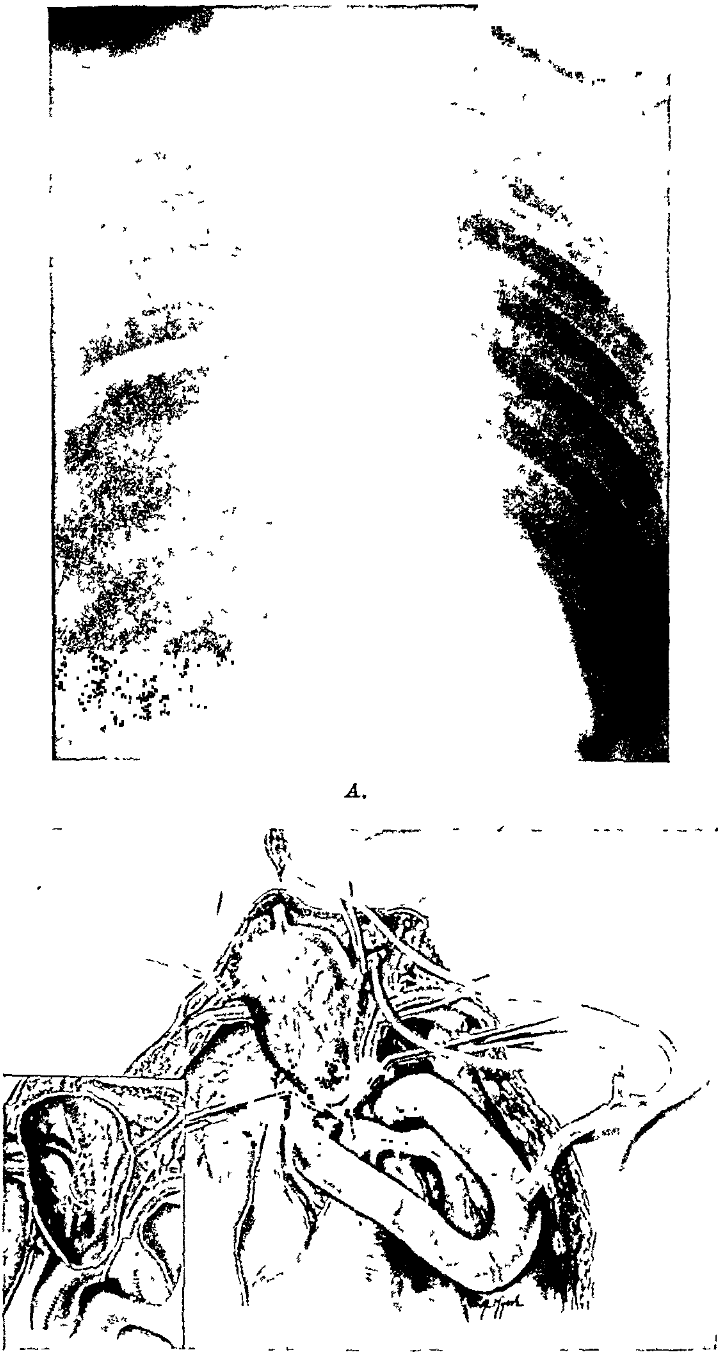
Complications as a result of occlusion of the descending thoracic a
pend upon the level of occlusion, whether occluded at two levels simulta
duration of occlusion, division of intercostal arteries, and extent
laterals[1, 16, 17]

It has been demonstrated that the duration of aortic occlusion can b
extended by the use of hypothermia[17] and, also, that the use of temp
permanent bypass shunts eliminates the dangers of aortic occlusion.[3,
does not, however, eliminate the dangers of cord ischemia as a result of
of intercostal arteries at the site of the aneurysm It is entirely likely, l
that the presence of the aneurysm has stimulated the development of col

CASE 5—M W, a 65 year old Negro woman, had a grapefruit sized saccular aneurysm of the upper descending thoracic aorta The aneurysm had eroded the thoracic vertebral bodies and compressed the trachea and esophagus (Fig 5, *A*). Exposure was obtained through a bilateral thoracotomy A compressed Ivalon graft, 2 cm in diameter, was inserted by end to side anastomosis as a shunt from the arch to the distal descending aorta, allowing aneurysmectomy to be accomplished without haste (Fig. 5, *B*) The lower trachea was noted to be quite soft and flexible at the site of its compression. The patient tolerated the surgery well, but 18 hours later developed respiratory distress The clinical picture suggested heart failure but therapy directed along these lines did not alter her deterioration There was no significant elevation in blood pressure in the arms to suggest increased resistance from the shunt. Autopsy revealed pronounced pulmonary congestion consistent with heart failure and marked collapse of the lower trachea Her death presumably was due to heart failure aggravated by hypoxia resulting from the collapsing trachea

CASE 6—O K, a 60 year old white man, had a long fusiform aneurysm involving two thirds of the descending thoracic aorta (Fig. 6, *A* and *B*) The surgical approach was through a long left parascapular incision with pleural entry through the bed of the resected fourth rib for mobilization of the proximal portion of the aneurysm and through the bed of the resected eighth rib for exposure distally A permanent compressed Ivalon sponge graft was placed end to side between the arch and the supradiaphragmatic portion of the aorta, with subsequent aneurysmectomy (Fig 6, *C* and *D*). The postoperative course was benign and the patient presented no evidence of neurologic damage He was doing well when last seen 13 months after surgery

Aneurysms in the distal thoracic aorta may make surgical repair quite hazardous because the great radicular artery to the anterior spinal artery arises at this level[1, 19] It presumably arises in the eighth to twelfth thoracic segment and, if these intercostals have to be divided, serious neurologic sequelae may result The presence of the aneurysm, however, with perhaps thrombosis of some of the intercostals, may provide adequate stimulus for development of collaterals In the absence of a shunt or hypothermia, renal damage then becomes with two No. 16 F. plastic catheters which were inserted into the carotid arteries, the right in the neck and the left within the thorax (Fig. 4, *B*). The arch was then isolated by occlusive clamps while circulation was maintained to all organs through the shunt. The femoral artery pressure, which was being monitored with a Statham transducer and Cambridge recorder, did not change with aortic occlusion and remained at about 100 mm. Hg systolic during the hour on the bypass. Cardiac function seemed good during the bypass, indicating



A.

B.

Fig. 4.—*A*, Posteroanterior x-ray of chest which shows innominate artery aneurysm extending into neck. *B*, Drawing which shows temporary bypass graft to provide blood flow to brain and distal organs during reconstruction of aorta.

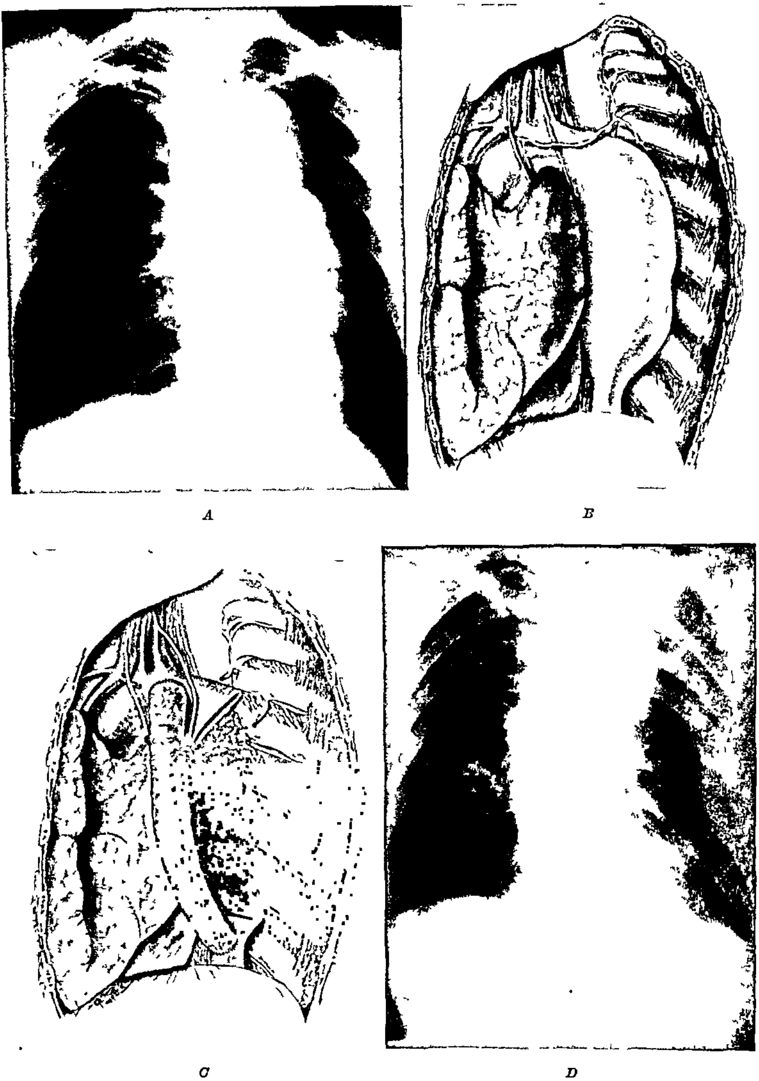


Fig 6 —Posteroanterior x-ray of chest (*A*) and drawing (*B*) which show fusiform aneurysm involving two thirds of the descending thoracic aorta.

Drawing which shows permanent compressed Ivalon sponge bypass graft (*C*) and postoperative x-ray (*D*).

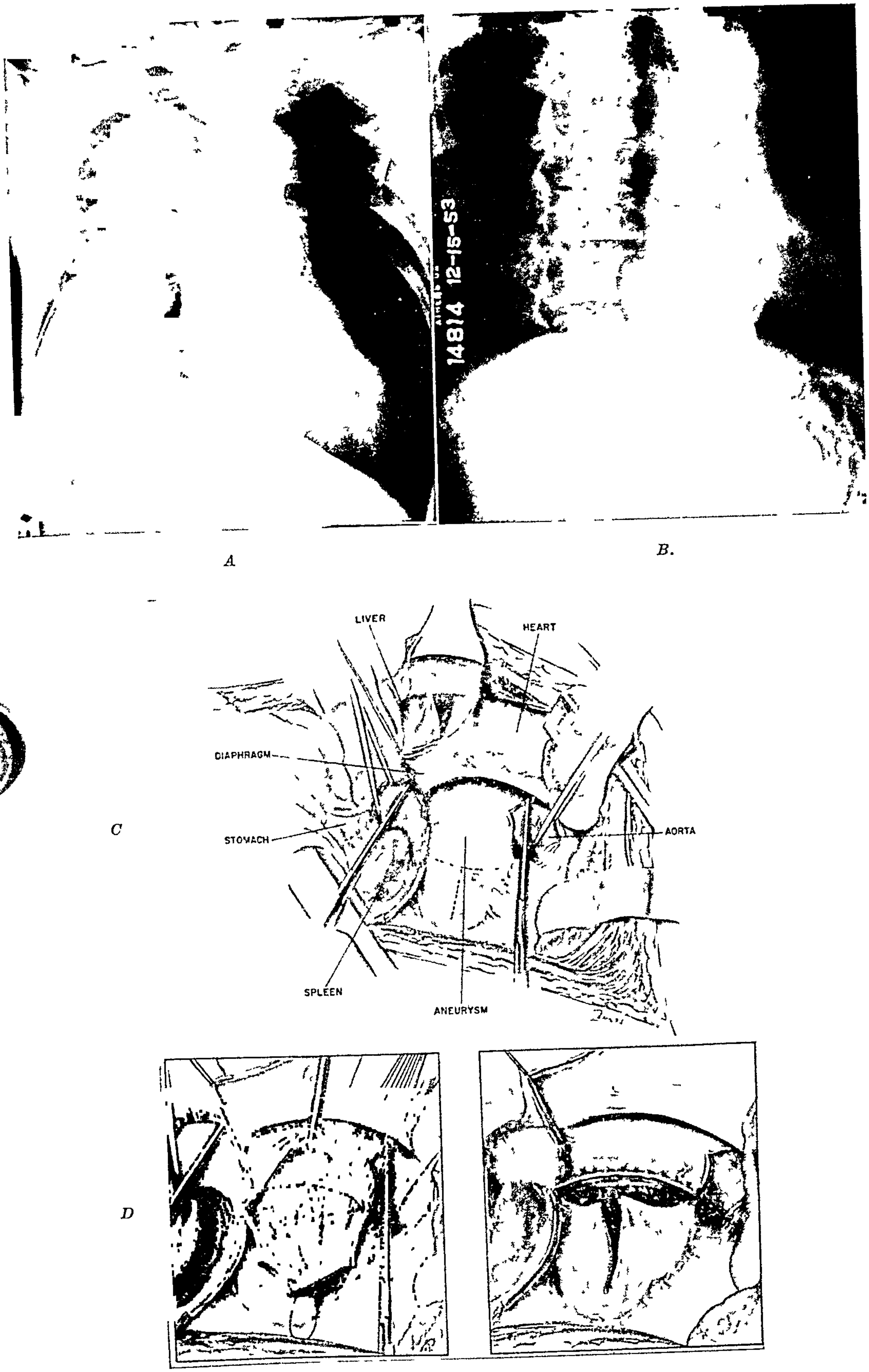


Fig 7.—*For legends see opposite page.*

Case 7.—H. W., a 63-year-old white man, had a saccular aneurysm of the thc just above the diaphragm (Fig. 7, *A* and *B*). It had eroded the eleventh and tw bral bodies. Exposure was obtained through a long left thoracoabdominal incis careful mobilization of the aorta just above and below the aneurysm, the aorta w for 40 minutes while a restorative endoaneurysmorrhaphy was done. The exce excised (Fig. 7, *C* and *D*). No neurologic damage was evident but the patient d

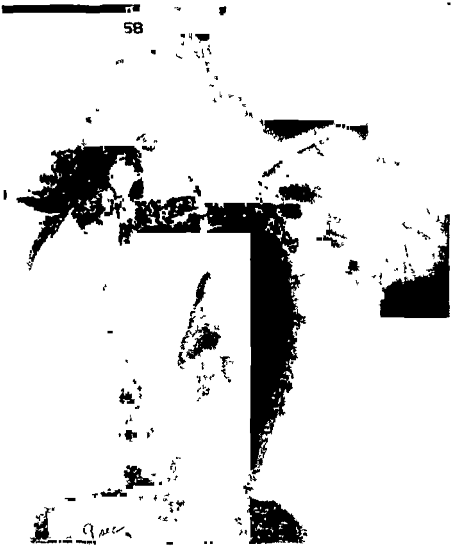


Fig 8 —*A*, Aortogram showing fusiform aneurysm of ascending aorta and saccular aneurysm of upper descending aorta

oliguria with an NPN elevated to 70 which had returned to normal when he had been dismissed 2 weeks postoperatively. An aortogram made by injection of 50 c.c. of 70 per cent Urokon intravenously, prior to dismissal, revealed that the reconstructed aorta had a slightly larger diameter than the aorta proximally. This discrepancy, of course, is undesirable because of the greater lateral pressure in this area. When the patient was seen recently, 3 years since the repair, he was found to have an aneurysm in the same area about the size of the original one. He refused surgery which would have consisted of replacement with a graft.

In such cases, a bypass graft anastomosed end-to-side to the aorta prior to excision of the aneurysm probably functions as well as one sutured end-to-end to the aorta. Since many of these patients have other serious organic diseases, the greater operating time in the latter case may work to a disadvantage for the patient.

Case 8.—C. C., a 62-year-old white man, had a left exploratory thoracotomy performed elsewhere, because of suspected bronchogenic carcinoma. He was found to have a saccular aneurysm involving the upper descending thoracic aorta presenting into the hilus of the left

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Fig. 7.—*A* and *B*, Posteroanterior and oblique x-rays showing saccular aneurysm just above the diaphragm and eroding the eleventh and twelfth vertebral bodies.
C and *D*, Drawings which show method of lateral reconstruction

lung with obstruction of the left main-stem bronchus and partial atelectasis of the left lung. He was also found to have a smaller aneurysm of the ascending aorta. X-ray study, including angiocardiography, confirmed the presence of the two aneurysms (Fig. 8, *A*); because of symptoms of cough, wheezing and shortness of breath associated with bronchial obstruction, a surgical attack upon the more distal aneurysm seemed urgent. The aneurysm was exposed through a left posterolateral incision and proximal and distal control obtained by encircling umbilical cord tape. Partial cardiopulmonary bypass was utilized to provide adequate blood flow distally as well as to avoid the hazards of increased pressure in the proximal aortic segment during aortic occlusion.[14] For this purpose, a stainless steel cannula was placed in the left subclavian artery from which blood was pumped through a De Bakey roller pump into a femoral artery. Monitoring pressures were obtained through a catheter in the right radial and other femoral artery. During 50 minutes of partial bypass, the neck of the sac was mobilized and a lateral reconstruction accomplished. In the base of the sac, the left main-stem bronchus was identified with an ulcerated defect, 1 cm. in diameter. This defect was repaired by suturing a graft of Teflon cloth snugly over the defect which was reinforced by two layers of the tough aneurysmal sac (Fig. 8, *B* and *C*). The surgical procedure was tolerated extremely well and the postoperative course was benign. The left lung promptly re-expanded and symptoms associated with bronchial obstruction have been completely relieved.

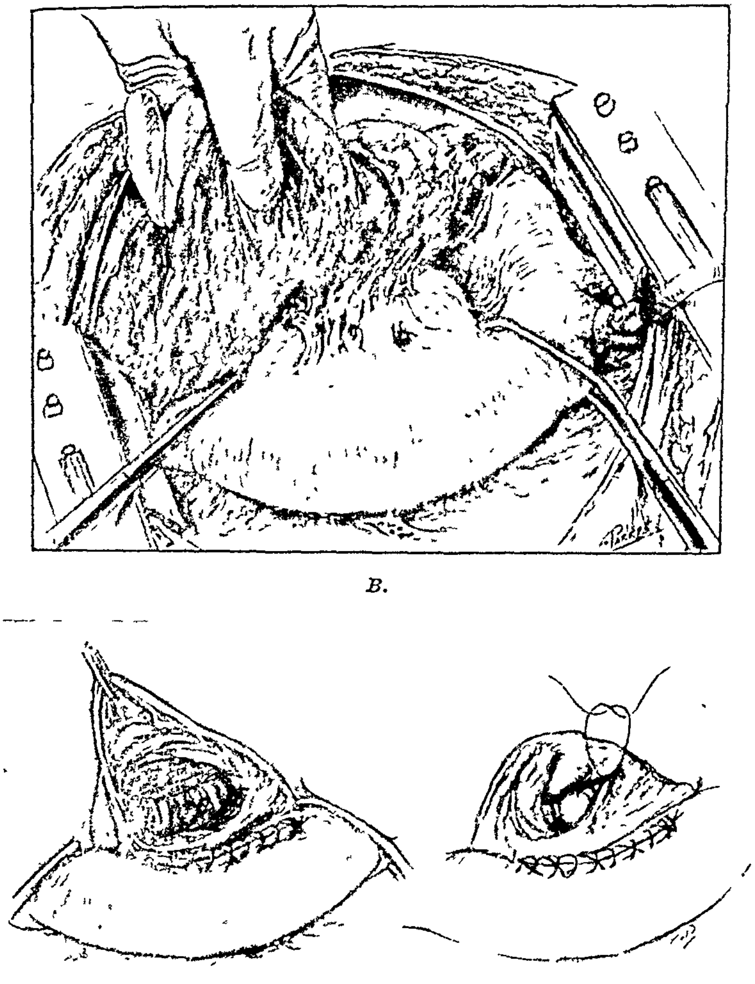

Fig. 8.—Cont'd. *B* and *C*, Drawings which show saccular aneurysm of descending aorta extending into hilus of lung and eroding left main-stem bronchus

SUMMARY

The major problems to be overcome in the surgical treatment o aortic aneurysms are concerned with the ill effects, both proximally an of having to stop the flow of blood through that portion of the aorta, the technical aspects of the actual repair Case histories of patients il many of these difficulties are presented Methods are presented whic used in securing adequate surgical exposure, in avoiding some of th associated with cross clamping the aorta, and in carrying out the aspects of aortic replacements

Further improvement in the results of surgery of this type is pected with simplification and more common usage of temporary shunts and with the utilization of pump oxygenators in certain circu

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PERFORATION OF THE RIGHT VENTRICLE DURING SELECTIVE ANGIOCARDIOGRAPHY

Report of a Case

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THE RECENT literature contains several reports attempting to evaluate the indications and technique of selective angiocardiography.[1-4] Critical evaluation of such a technique should include a consideration of the potential dangers and complications. Included in the rarer complications is perforation of the heart. The true incidence of this mishap is difficult to determine. Bagger and her associates,[1] in a review of 2,958 selective angiocardiograms from 12 Swedish hospitals, reported four instances of injection of contrast material into the right ventricular myocardium. Escher, Shapiro, Rubinstein, Hurwitt, and Schwartz[5] described actual perforation of the right ventricular apex with partial injection of contrast material into the pericardial cavity in a 27-year-old woman with isolated pulmonic stenosis. Cardiac tamponade ensued, necessitating pericardiotomy. Because selective angiocardiography is increasing in popularity in this country, the following case is deemed worthy of record.

CASE REPORT

The patient, a 26-month-old white female, was admitted to the hospital on Jan. 1, 1958, for evaluation of congenital heart disease. She was born following a full-term uneventful pregnancy. Birth weight was 6 pounds 11 ounces. Cyanosis was noted shortly after delivery. Development was slow, and repeated respiratory infections required frequent hospitalizations. The child did not walk until 2 years of age and was noted to squat when fatigued. The slightest exertion produced marked dyspnea and accentuated a persistent mild cyanosis.

Physical examination on admission revealed a pale, poorly developed, scrawny 2-year-old girl, weighing only 17 pounds. There was cyanosis of the lips and nail beds at rest. The chest was symmetrical and the lungs clear. Cardiac rate was 136 with a loud harsh systolic murmur audible over the third and fourth intercostal spaces along the left sternal border. A thrill accompanied the murmur. The pulmonic second sound was louder than the aortic. Femoral pulses were easily palpable. A smooth, nontender liver edge was felt 1 cm. below the right costal margin. There was clubbing of the fingers and toes but no peripheral edema. Hemoglobin was 16.1 Gm. with an hematocrit of 67 per cent. An electrocardiogram was interpreted as showing right ventricular hypertrophy. Fluoroscopic and radiographic examination of the chest with barium swallow demonstrated a right-sided aortic arch, marked right

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ventricular enlargement, and prominent pulmonary vessels. The cardiac wai
narrowed but it was difficult to determine how much of this could be attributed
sided aorta.

On Jan. 21, 1959, a diagnostic cardiac catheterization and angiocardiogra
formed commencing at 1:30 P.M. Following sedation with 15 mg. of Demerol a
of Phenergan, a No. 6 N.I.H. cardiac catheter was passed without difficulty
antecubital vein into the right atrium. The patient had to be given oxygen by
after the procedure started because of increasing cyanosis. Her condition impro
catheterization was continued. During the procedure, the catheter passed throu
atrial septal defect into the left atrium and then into a left pulmonary vein.
was also passed from the right ventricle into the aorta but never into the pulmo

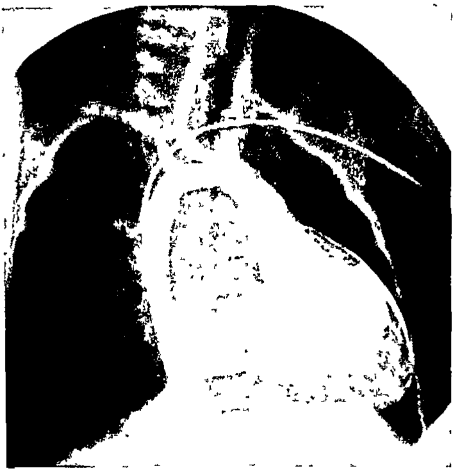

Fig 1.—Early angiocardiographic film showing contrast material in the pericardial cavity. Note the transposed aorta and failure of pulmonary vessel opacification.

Pressures in the aorta were 58/28 mm. Hg and in the right ventricle 56/5-10 mm. Hg. The catheter tip was then placed deep in the apex of the right ventricle. The diagnostic catheterization itself concluded at 3:00 P.M.

The patient was placed in a slight left posterior oblique position on a Schönander serialographic film changer. A preliminary film showed no change in the location of the catheter tip. The condition of the patient seemed satisfactory with continuous oxygen therapy.

At 3:20 P.M., 8 ml. of 90 per cent Hypaque was injected using a pressure of 10 Kg. per square centimeter. The injection lasted slightly over 2 seconds and was well tolerated. Films were taken at a rate of six per second for 2 seconds followed by four per second for 4 seconds. Continuous electrocardiographic monitoring showed no significant changes. Therefore, the catheter was left in place during the 10 minutes required for developing and viewing of the films. On viewing the films, it was obvious that part of the contrast medium was in the myocardial wall and pericardial cavity. A lateral film was immediately obtained to verify the catheter position and an attempt was made to aspirate the pericardial cavity via the catheter. Less than 2 cm. of dye was obtained, followed by bright red blood. The catheter was carefully withdrawn. Auscultation of the heart by members of the cardiac surgery team present during the injection disclosed a loud pericardial friction rub. The quality of the heart tones, however, seemed unchanged.

Careful monitoring of the pulse and blood pressure was begun and the operating room alerted. However, the patient's condition remained stable. A chest film 30 minutes after the injection showed some residual dye in the pericardial cavity but no significant change in cardiac size or contour. At 4:45 P.M., the patient was transferred to her room where the constant surveillance was continued. Her vital signs and general condition remained stable.

Chest films the following morning showed complete disappearance of the contrast medium and no change in the cardiac silhouette. An electrocardiogram showed a 2:1 auriculoventricular block but no changes suggestive of pericarditis. The remaining hospital course was uneventful and the patient was discharged from the hospital on Jan. 28, 1959.

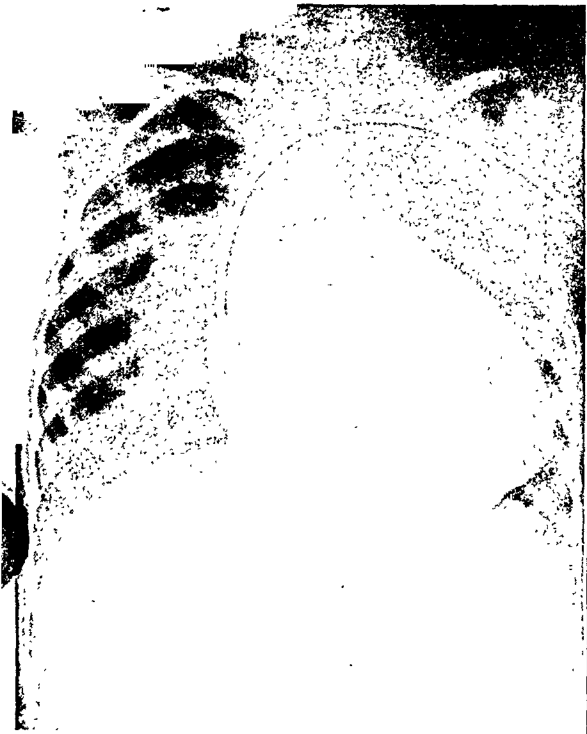

Fig. 2.

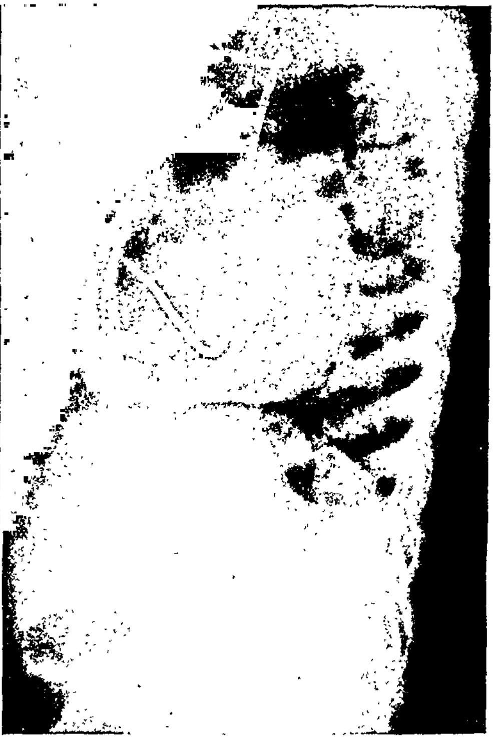

Fig. 3.

Fig. 2.—Chest film just prior to catheter withdrawal.
Fig. 3.—(Lateral of Fig. 2.) Note residual dye in pericardial cavity.

Angiocardiography confirmed the clinical impression of complete transposition, demonstrating aortic filling from the right ventricle and a right-sided descending aorta. A left innominate artery was also present. At no time was any contrast material seen in the pulmonary vessels.

DISCUSSION

Selective angiocardiography offers definite advantages over venous techniques in the diagnosis of congenital cardiac lesions. Among the latter are the ability to use less contrast medium, precise placement of the contrast agent, and elimination of superimposition. As ordinarily performed, this technique is associated with a minimal morbidity and mortality,[1] in spite of the poor general condition of many of the subjects.

Perforation of the heart is a serious though fortunately rare cor
Using closed tipped, relatively wide bored, side opening catheters, th
of recoil and high pressure jets encountered with the older Cournanc
has been partially solved However, the newer type catheter intrc
difficulty of precise localization with pressure and oxygen deter
because of the multiple holes proximal to its tip One opening suffice
blood samples but the exact localization of the 2 cm of catheter di
most proximal hole can only be inferred from fluoroscopy and film
and his co workers[5] have pointed out, the advantages of the N I H
justify the risk of its use and certain precautions can be taken to r
risk to a minimum

Blind manipulation of the catheter should be avoided If necessa
scout films should be taken prior to injection Hilbish and Mor
emphasized this in presenting a case in which withdrawal of the (
inches failed to change the position of the catheter tip in the pulmona
Tightening of the intracardiac loop with no change in position of
catheter can only be detected by repeat films or fluoroscopy

The time during which the catheter remains unchanged in positi
the heart should be reduced to a minimum Subendocardial hemorr
mural thrombus formation have been observed in dogs following cathet
but are probably uncommon in human beings Nonetheless, prolong
between positioning and injection increase the risk of endocardial damage

In our case, the most important factor conducive to perforation is considered to be the position of the catheter To advance the catheter deep into the apex of the right ventricle places the tip against the junction of septum and ventricular wall The slight apical elevation accompanying each systole may impale the thin right ventricular apex against the rigid, relatively sharp tipped N I H catheter It is easy, under these circumstances, to visualize perforation of the endocardium with insinuation of the catheter between the myocardial fibers The more energetically the catheter is secured in the right ventricular apex and the longer it is left in this position, the greater the likelihood of this complication In studying right ventricular outflow tract problems, our current policy is to advance the catheter tip well into the outflow tract so that its course describes the characteristic U shaped configuration After positioning, one should be able to freely advance or withdraw the catheter *a distance of a* few centimeters If a more proximal injection is desired, for example, to demonstrate an interventricular septal defect, the catheter tip is positioned slightly distal to the atrioventricular valve as determined by pressure readings Under no circumstances should the catheter be advanced until resistance is met and left deep in the right ventricular apex Such a technique, especially in the thin walled right ventricle of infants, entails an additional unnecessary risk If a satisfactory U shaped bend cannot be achieved in studying right ventricular outflow problems, the catheter should be withdrawn proximally under fluoroscopic control to a point just distal to the tricuspid valve

The treatment in this case was wholly expectant. Aspiration through the catheter prior to its removal undoubtedly failed to recover all of the pericardial fluid. Serial chest films are of little value for, as Escher and her colleagues[5] have pointed out, the volume of pericardial fluid producing acute tamponade is close to the minimal amount that can be visualized roentgenographically. Frequent observations of the clinical signs and symptoms provide the best guide to therapy. Should tamponade develop, pericardicentesis or open pericardiotomy may be required. However, many of these patients are poor surgical risks by the very nature of their disease and the conservative therapeutic approach should be given first consideration.

SUMMARY

A case of perforation of the right ventricle during selective angiocardiography has been presented. Possible contributory factors, especially the positioning of the catheter, have been considered. Recommendations are made to help avoid this complication.

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BILATERAL SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS

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SINCE the early optimistic reports,[1-5] bilateral resection for pulmon culosis has gained considerable acceptance. However, opinions garding the indications, results, and risks of the procedure. With few e reported series are small and usually include carefully chosen pati little disease.[6-10] A number of surgeons and phthisiologists believe pulmonary resection to be less successful than unilateral resection.[12] differences of opinion exist regarding the applicability of procedure bilateral thoracoplasty and Monaldi cavernostomy,[13] neither of which l popularity.

It is the purpose of this paper to review the experience at the R State Tuberculosis Hospital with bilateral surgical procedures, inclu naldi cavernostomy, thoracoplasty, pulmonary decortication, and resec attempt to evaluate them.

Since July 1, 1949, 103 patients have completed bilateral surgery. three patients had bilateral pulmonary resection, of which 164 were performed at Ray Brook, and 3, prior to admission. Two of the patients had 3 resections each. Four of the patients were admitted to Ray Brook with thoracoplasties. Twenty patients were treated with miscellaneous surgical procedures listed in Table II.

In this series there were 59 males and 44 females. Sex does not seem to be an important consideration in selecting patients for operation; nor does it seem to influence results to an appreciable extent. Ninety-five of the 103 patients in this series, or 94 per cent, were under the age of 50 years at the time of the last surgical procedure. Only 1 patient was over 60 years of age. Age distribution was similar in the bilateral resection and miscellaneous bilateral surgery groups.

BILATERAL PULMONARY RESECTION

The first bilateral pulmonary resection was completed in December, 1951. A total of 164 procedures are summarized in Table I. Two of these were simultaneous. Since bacteriology, extent of disease, antituberculous drug therapy, and type of surgery can be expected to influence results, this information is listed. "New" drugs include pyrazinamide, cycloserine, viomycin, kanamycin,

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Table I. Bilateral Pulmonary Resections

	NUMBER OF PROCEDURES	EXTENT OF DISEASE*			DRUGS ADMINISTERED AT OPERATION†			OPERATIVE PROCEDURE‡				COMPLICATIONS		
												EARLY		
		MINIMAL	MODERATE	FAR-ADVANCED	SM, PAS, OR INH	"NEW"	NONE	P	L	S	W	TUBERCULOUS	NON-TUBERCULOUS	LATE TUBERCULOUS
Patients harboring culturable tubercle bacilli§	48	1	23	24	18	27	3	1	18	10	19	6	1	4
Patients harboring no culturable tubercle bacilli	116	7	84	25	109	6	1	0	7	26	83	0	2	1
Total	164													

*National Tuberculosis Association classification.

†SM = Streptomycin; PAS = para-aminosalicylic acid; INH = isoniazid.

‡P = Pneumonectomy; L = lobectomy with or without segmental and/or wedge resection; S = segmental with or without wedge resection; W = wedge.

§Resected tissue and/or expectorations.

Promizole, and Tibione Only drugs to which the patient's organisms proved susceptible are listed Tubercle bacilli are considered susceptible to streptomycin or para aminosalicylic acid if they do not grow in the presence of 10 mcg per milliliter, and to isoniazid if they do not grow in the presence of 5 mcg per milliliter Details of susceptibility tests have been described elsewhere[14] Tubercle bacilli are considered susceptible to the "new" drugs if the patient has not previously received them Early tuberculous complications include empyema or spread of disease occurring within a period of 1 month following surgery Nontuberculous complications include hemothorax, nontuberculous empyema, and transient increases in abnormal shadows in the postoperative roentgenogram Pleural "space problems" are not listed, but an indication of their frequency may be surmised from the fact that 21 postresection thoracoplasties were performed It should be noted, however, that early in this series some thoracoplasties were performed to prevent overdistention of the residual lung tissue At present, thoracoplasty is employed only to obliterate residual pleural spaces or empyemas Late tuberculous complications include reappearance of culturable tubercle bacilli in the expectorations or increase in disease by roentgenogram after the first postoperative month

From general experience it is to be expected that patients who have extensive disease and harbor culturable tubercle bacilli would have more tuberculous complications than those who do not[15] Table I shows that there were no early tuberculous complications and only one late bacteriologic relapse in the group of patients who did not harbor culturable tubercle bacilli In 6 early tuberculous cases, complications occurred in 5 patients who harbored viable bacilli and included 5 empyemas and 1 spread of disease Two of these patients received no effective drug therapy Two received "new" drugs and 1 received para aminosalicylic acid alone Further surgery in the form of pulmonary resection decortication and thoracoplasty succeeded in curing 2 patients of their complications Nontuberculous complications included 2 transient increases in abnormal shadows on the postoperative roentgenogram and 1 staphylococcal empyema The latter was successfully treated by thoracentesis and antibiotics The late tuberculous complications included 5 bacteriologic relapses accompanied in 2 instances by changes in chest roentgenogram and in 1 instance by ulceration of the stump of a resected bronchus Three of the 5 patients who suffered relapses received "new" drugs and 1 refused to take antituberculous drug therapy after the first postoperative month Further antituberculous drug therapy succeeded in eliminating tubercle bacilli from the expectorations of 2 of the 3 patients who did not have changes in the chest roentgenogram One of the other 2 patients responded satisfactorily to additional pulmonary resection There was only one death, due to "heart failure," which occurred approximately 4 years after the last surgical procedure had been performed Thus, of the 83 patients, many of whom had advanced disease, 82 are living and 77 (94 per cent) have stable roentgenograms and expectorations free of tubercle bacilli

As every effort was made to conserve functional lung tissue, it is not surprising that pneumonectomy and lobectomy were performed in only 26 instances In patients with extensive disease, the surgeon may be forced to limit

TABLE II. MISCELLANEO[illegible]TERAL SURGICAL PROCEDURES

PROCEDURES	NUMBER OF PATIENTS	EXTENT OF DISEASE*			PATIENTS HARBORING CULTURABLE TUBERCLE BACILLI		ANTITUBERCULOUS DRUGS AT TIME OF SURGERY		RESULTS		
		MINIMAL	MODERATE	FAR-ADVANCED	YES	NO	YES	NO	STABLE ROENTGENOGRAM AND EXPECTORATIONS FREE OF TUBERCLE BACILLI	UNSTABLE ROENTGENOGRAM OR EXPECTORATIONS CONTAINING TUBERCLE BACILLI	DEAD
Resection + contralateral exploration	1			1	1		1				1
Resection + contralateral Monaldi	2			2	2		2		2		
Resection + contralateral standard thoracoplasty	4†			4	3	1	4		3		1
Bilateral resection + unilateral modified Schede	1‡			1	1		1			1	
Monaldi + standard thoracoplasty + contralateral resection	1§			1	1		1		1		
Resection + decortication + standard thoracoplasty	2		1	1	1	1	2		2		
Resection + decortication + plombage thoracoplasty	1		1			1	1		1		
Bilateral plombage thoracoplasty + resection + contralateral decortication	1			1	1		1				1
Bilateral standard thoracoplasty and unilateral Monaldi	1‖			1	1		1				1
Bilateral plombage thoracoplasty + unilateral Monaldi	1			1	1		1			1	
Bilateral standard thoracoplasty + bilateral Monaldi	2			2	2				1		1
Bilateral standard thoracoplasty	3		1	2	3		1	2	2		1
Total	20										

*National Tuberculosis Association classification.

†Thoracoplasties were performed prior to admission.

‡One resection was performed prior to admission.

§Monaldi and thoracoplasty were performed prior to admission.

‖One thoracoplasty was performed prior to admission.

resection to cavity-bearing tissues, leaving behind considerable a nodular disease. The technical aspects of this problem have been Occasionally, it may be impossible to identify pulmonary cavities preoperative roentgenogram or palpation at exploration. Under suc stances, the part of lung suspected of bearing a cavity can be incise danger. Bleeding from the lung is easily controlled by Allis clam also, cavities can be inspected to determine whether or not they contai material or are lined by a smooth, glistening membrane. The risk tamination of the pleural cavity is minimal when antituberculous administered postoperatively.

Because of the unfavorable effect on pulmonary function, tho should be avoided whenever possible. Although postresection pleural should be eliminated without delay in patients harboring viable tuber they may be observed with little risk for considerable periods of t culturable tubercle bacilli have not been recovered from the sputum at the time of operation.

In the 80 patients who had both operations performed at Ray disease in each lung was equal in 39 patients. In the remaining pat had unequally distributed disease, the more diseased lung was oper first in 20 instances. Decisions regarding the side to be operated upon generally not influenced by the bacteriologic studies of the expectora extent of disease, or antituberculous drugs administered. No difference in results can be demonstrated between the group in which the worst side was operated upon first compared with the group in which the worst side was operated upon last. It would, therefore, seem unimportant which side is chosen for the first operation. The only exception appears to be the patients with a functionless lung who harbor viable tubercle bacilli, since they require extensive space-filling thoracoplasty following pneumonectomy. Since thoracoplasty tends to reduce pulmonary function even if performed over an empty pleural cavity or a functionless lung,[16] it should be performed only after the contralateral resection has been completed and function on that side has recovered to a considerable extent.

In this series, the interval between resections has varied considerably. For several years the second resection has been performed as soon as the patient's vital capacity has recovered sufficiently to tolerate another procedure, other factors being equal. Patients with exceedingly good function may easily tolerate simultaneous bilateral resection, which was accomplished in 1 patient in this series. It has been our experience that following pulmonary resection the vital capacity has recovered to a considerable degree by the sixth postoperative week.[17]

MISCELLANEOUS BILATERAL SURGICAL PROCEDURES

Various combinations of surgical procedures performed upon 20 patients are listed in Table II. These included Monaldi cavernostomy, various types of thoracoplasty, pulmonary decortication, and pulmonary resection. It will be noted that a proportion of these patients had extensive disease and harbored culturable tubercle bacilli in their expectorations. A number of these patients, too ill for bilateral pulmonary resection, were treated by plombage thoracoplasty and/or Monaldi cavernostomy. Twelve (60 per cent) are now alive with stable roentgenograms and expectorations free of tubercle bacilli. Two patients still have cavitary disease and viable tubercle bacilli in their expectorations. Six (30 per cent) are dead. Two patients died of pulmonary insufficiency within a few weeks following surgery, 1 died of a "heart attack" approximately 3 years after the last operation, 1 died in uremia due to amyloidosis approximately 3 years after pulmonary resection, 1 died of liver toxicity, probably the result of pyrazinamide intoxication, and 1 died a few hours after surgery following cardiac arrest on the operating table. Nonfatal complications in this group of patients consisted of 1 (tuberculous) infected plomb requiring evacuation of foreign bodies, and 1 hemothorax requiring re-exploration.

TABLE III. FUNCTION STUDIES

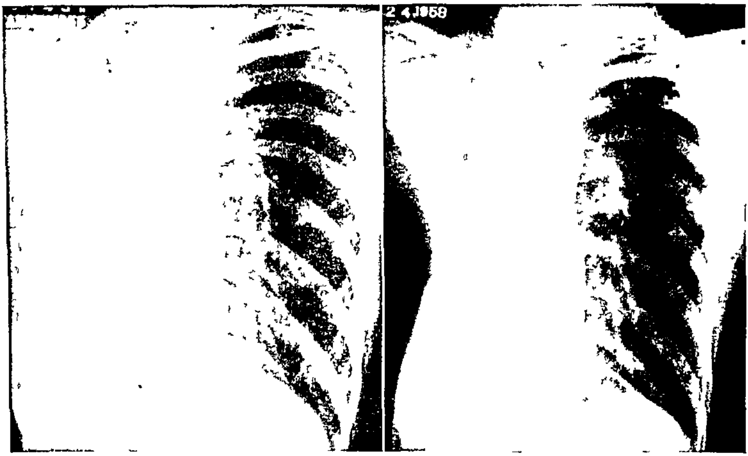
	NUMBER OF PATIENTS		PREOPERATIVE VITAL CAPACITY		POSTOPERATIVE VITAL CAPACITY (PER CENT PREOPERATIVE VALUE)	
	M	F	M	F	M	F
Bilateral resection + bilateral standard thoracoplasty	1		3,600		2,000[*] (56%)	
Bilateral standard thoracoplasty	1		4,450		2,260[†] (59%)	
Bilateral resection + unilateral standard thoracoplasty	4	3	2,360	2,480	1,930[‡] (82%)	1,630[§] (66%)
Resection + contralateral Schede thoracoplasty		1		1,850		1,300[¶] (70%)
Bilateral resection	18	6	3,490	2,520	3,060 (87%)	1,960 (77%)
Resection + contralateral Monaldi	1		3,500		3,200 (92%)	
Monaldi + contralateral decortication + thoracoplasty	1		2,800		2,700[‖] (96%)	
Resection + contralateral decortication + plombage		1		1,500		1,600[#] (107%)
Bilateral plombage thoracoplasty	1	1	1,800	1,300	1,800[**] (100%)	1,100[††] (85%)
Bilateral resection + unilateral decortication	1		2,000		2,450 (123%)	
Totals	28	12				

[*] Five ribs removed bilaterally.
[†] Bilateral 6-rib thoracoplasty.
[‡] Nine ribs, 4 ribs, 3 ribs, and 2 ribs removed, respectively.
[§] Four ribs removed from each of 2 patients and 3 ribs from the other.
[¶] Four-rib modified Schede thoracoplasty.
[‖] Four-rib standard thoracoplasty.
[#] Five ribs.
[**] Five ribs on one side and 7 on the other.
[††] Six ribs on one side and 8 ribs on the other.

PULMONARY FUNCTION

Table III summarizes the effects of various combinations of surgical procedures upon the vital capacity. Postoperative determinations were accomplished 2 months or more following the last procedure. Undoubtedly operative values might have been somewhat higher if longer period had been permitted to elapse following surgery, but it is believed that is sufficient time to permit recovery of a major portion of postopera tion.[18] Bilateral plombage thoracoplasty was surprisingly innocuous pulmonary resection was followed by a decrease of approximately 20 in vital capacity. As might have been expected, Monaldi cavernos relatively innocuous, and pulmonary decortication was sometimes fo improvement in function. These results are similar to those of Gae Strieder.[19]

It is impossible to define the lower limits of pulmonary function permit bilateral pulmonary surgery. In borderline cases the decis the second operation should be postponed until it is determined that th has tolerated the first procedure well. Case 1 is an example of a pa did well in spite of poor pulmonary function



A *B*

Fig 1—*A*, Preoperative roentgenogram revealing destroyed right lung which contains a large cavity with a fluid level There is cavitary disease in the upper left lung field *B*, Roentgenogram following bilateral pulmonary resection and right thoracoplasty

CASE REPORT

CASE 1.—F. T., a 24 year old man, was admitted to Ray Brook State Tuberculosis Hospital on April 24, 1954, with far advanced active pulmonary tuberculosis Known onset of pulmonary disease was December, 1947, when an abnormality in the right lung was noted He was treated by a rest regimen In March, 1953, the patient developed fever and productive cough accompanied by fatigue and weight loss Roentgenograms revealed evidence of extensive disease in the right lung and expectorations contained tubercle bacilli. Streptomycin, isoniazid, and para aminosalicylic acid were prescribed, but the latter drug was stopped because of fever and rash.

Admission roentgenograms of the chest at Ray Brook (Fig. 1) revealed complete destruction and cavitation of the right lung and evidence of 2 small cavities in the outer first and second anterior interspaces on the left. Tubercle bacilli recovered from the patient's expectorations grew abundantly in 10 mcg. per milliliter of streptomycin and 5 mcg. per milliliter of isoniazid. The patient was gradually desensitized to para-aminosalicylic acid and full dosage of 12 grams a day was reached by Aug. 22, 1954. On March 18, 1955, pyrazinamide, 1 gram 3 times a day, was started. On March 28, 1955, a wedge resection of the cavity-bearing portion of the left lung was performed. The postoperative course was uncomplicated. On June 6, a right pleuropneumonectomy was accomplished. On June 13, it was necessary to do a temporary tracheotomy to maintain the tracheobronchial tree free of secretions. On July 25, a 9-rib right thoracoplasty was performed. Postoperatively the patient did well except for the reappearance of tubercle bacilli in the expectorations of Jan. 25, 1956. Bronchoscopy revealed redness and edema of the stump of the right main bronchus. Expectorations continued intermittently to yield tubercle bacilli. On Nov. 9, 1956, bronchograms failed to reveal evidence of a fistula or pleural pocket connected with the stump of the right main bronchus. On Nov. 17, 1956, pyrazinamide and para-aminosalicylic acid were discontinued and tetracycline, 250 mg. 4 times a day, and cycloserine, 250 mg. twice a day, were substituted. The latter drugs were continued until Jan. 16, 1958. The patient continued to discharge viable tubercle bacilli until Jan. 21, 1957, after which bacilli could not be identified. Tubercle bacilli recovered from the resected right lung grew abundantly in the presence of 10 mcg. per milliliter of para-aminosalicylic acid. Vital capacity on March 7, 1955, was 2,100 c.c. and on March 17, 1958, it was 1,700 c.c.

The patient was discharged from the hospital on March 29, 1958, and until his last examination in October, 1958, had remained well. In May, 1959, he reported he was well and working.

DISCUSSION

A considerable proportion of the tuberculous complications which occurred following bilateral pulmonary resection may be attributed to poor antituberculous drug coverage. Even so, the results were remarkably favorable. These results were undoubtedly influenced by careful selection of patients for surgery. Indeed, perhaps selection was too careful, for a higher incidence of complications would have been acceptable if the benefits of bilateral resection could have been extended to more seriously ill patients. This assumption appears to be substantiated by the fact that the patients in this series with extensive disease who harbored viable tubercle bacilli responded well to surgery.

Generally, bilateral pulmonary resection with or without decortication or a small thoracoplasty offers the best opportunity for cure with relatively little permanent effect upon pulmonary function. However, since open thoracotomy is followed by a severe temporary decrease in pulmonary ventilation postoperatively,[17] it may be preferable to perform plombage thoracoplasty or Monaldi cavernostomy in patients with limited pulmonary function. These technical problems have been reviewed elsewhere.[15]

SUMMARY

One hundred and three patients with pulmonary tuberculosis have been treated by bilateral surgical procedures. The best results were obtained in the group of patients who had bilateral pulmonary resection. Other procedures

yielded good results considering the severity of the tuberculosis and con
diseases The effects of various combinations of surgical procedures ı
monary function are reviewed

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EXPERIMENTAL CHRONIC TUBERCULOUS PERICARDITIS

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Previously, we reported the experimental production of tuberculous pericarditis in animals by sensitization with heat killed bacilli followed by the intrapericardial injection of live bovine tubercle organisms. Typical tuberculous pericarditis developed in all animals which survived the immediate postoperative period. The animals were sacrificed at intervals, the longest being 3 months. No constrictive pericarditis was found. In the following study, the animals were kept for longer periods with the hope that the constrictive phase of tuberculous pericarditis would develop. To our knowledge, this has not been accomplished experimentally.

METHOD

Young New Zealand white rabbits were used. Approximately one half of the animals were injected with heat killed tubercle bacilli suspended in Bayol F and were later found to have positive intradermal tests for sensitivity. (Subsequently, it was felt that sensitization was unnecessary as the same degree of pericarditis developed.) Approximately 0.5 c.c. of a milky suspension of live bovine tubercle bacilli was injected into the pericardium after making a small incision in the left fourth or fifth intercostal space. A high postoperative mortality rate occurred in spite of careful wound closure. The animals were isolated but given no special treatment for their tuberculosis. Eighteen animals survived 6 months or longer. One animal died during the seventh month, 3 during the ninth month, and 4 during the tenth month after injection. Because of this increasing mortality, 5 animals were sacrificed during the eleventh month and 5 during the twelfth month. The latter group lacked 3 weeks of living 1 year after injection.

RESULTS

All animals had diffuse tuberculous pericarditis. In those animals sacrificed, after anesthesia had been obtained, the thorax was widely opened to observe the

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heart action and no evidence of constriction was found in any anim pericardium was usually slightly thickened and had lost the normal glos A small increase in the pericardial fluid was present Tubercle forma evident almost uniformly to a greater extent over the epicardium, partic the vicinity of the coronary vessels Tuberculosis was not found else the animals, although the brain was not removed

Microscopically, all stages of the granulomatous process were obse the main reaction consisted of lymphocyte and macrophage tubercle f A few giant cells were seen In every animal, and in practically ever made, at least one area of calcification was found but this was never area nor widespread in extent Fibrous tissue deposition was also not e

SUMMARY

Chronic tuberculous pericarditis was produced in rabbits by the i cardial injection of live bovine tubercle bacilli Animals surviving fro months showed an extensive granulomatous reaction with areas of calc osition but constrictive pericarditis was not produced

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PRE- AND POSTOPERATIVE CARDIOPULMONARY DYNAMICS OF THE EMPHYSEMATOUS BULLA

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Reports on giant emphysematous bullae have become increasingly frequent not only with respect to cases of successful treatment by surgery but also in the number of cases diagnosed roentgenologically.[4, 5, 16, 19, 20, 23, 24, 28, 29, 36] However, reports on the cardiopulmonary dynamics of the disease have been extremely few. Baldwin and her colleagues[6, 7] reported respiratory function in patients with emphysematous bullae with and without emphysema, and Siebens and his associates[32] made a report of cases of bullae without emphysema, but these authors failed to agree in the interpretation of the hypoxia associated with the giant bullae. As for cardiopulmonary dynamics, chiefly of the pulmonary circulation, FitzPatrick[21] reported a number of cases with and without emphysema. With reference to bullae without emphysema, there seems to have been no divergence of opinion as to the indications for operation, operative methods, and the results of physiologic investigation, but in the case of bullae with emphysema there has been confusion, not only as to indications for surgery but also in the results of physiologic investigation.

Out of 11 cases of giant bullae diagnosed by us, 8 patients were surgically treated and this report concerns the pre- and postoperative data of respiratory function and pulmonary circulation, the operative indications, and a more rational approach in the care of giant bullae.

MATERIAL AND METHODS

There were 11 cases of bullae larger than a child's head in size (Table I). In most cases several years had elapsed before any signs developed. Only 2 patients had shown symptoms of anoxia and hypercapnia to the point of incapacitation. Eight patients were operated upon. Segmental resection was usually applied, but in a few cases Naclerio-Langer's operation[25] was performed. After disposal of the bullae, the vagus nerve was divided in its trunk on the right, but when the affected side was on the left, vagotomy was performed in the portion distal to the emergence of the recurrent nerve, with division of its pulmonary branches at the hilus. Furthermore, a sympathectomy of the lung was

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TABLE I CLINICAL FINDINGS

CASE NO	AGE	CHIEF COMPLAINTS	OPERATION METHOD	FOL
137	32	Emaciation	Segmental resection, denervation, pleurectomy, and pleural poudrage	Well an ping
096	57	Bloody sputum, cough and palpitation under exercise		
119	60	Sputum, dyspnea, and palpitation under exercise	Segmental resection, denervation, pleurectomy and pleural poudrage	Better
162	45	Slight fever and emaciation	Segmental resection, denervation, and pleural poudrage	
012	23	Asthma attack dyspnea, and emaciation	Naclerio Langer's operation	Asthma
188	51	Sputum		
104	61	Cough and dyspnea		
220	43	Cough, sputum, and dyspnea	Segmental resection, denervation, pleurectomy, and pleural poudrage	Better symptomatically
224	52	Cough and sputum	Segmental resection, denervation, pleurectomy, and pleural poudrage	
088	48	Dyspnea, cough, and sputum	Naclerio Langer's operation, denervation and pleural poudrage	
152	44	Exertional dyspnea and emaciation	Naclerio Langer's operation, denervation, pleurectomy, and pleural poudrage	Asthma attack

performed by thoracic ganglionectomy (D_2-D_9), and a trial was made of parietal pleurectomy and pleural poudrage in accordance with the technique of Crenshaw and his associates[11, 12, 13]

All patients were discharged 4 to 8 weeks after the operation, and all were working full time a half year after surgical intervention Two patients with incapacitating symptoms and signs were greatly improved after the operation and resumed work The first patient was an exceptional one in whom only Naclerio Langer's operation had been performed, without denervation and pleural poudrage Severe asthma developed followed by a relapse 2 years after operation This was corrected by a second operation 3 years after the first one

METHODS OF MEASUREMENT

1 *Spirometric Measurements*—Spirometric measurements were taken of vital capacity (VC), minute volume (MV), the maximum breathing capacity (MBC), and oxygen consumption Minute volume was recorded as liters per minute per square meter of body surface Ventilatory equivalent was expressed by air volume to be ventilated due to consumption of 100 c c of oxygen as L unit (liters per 100 c c of oxygen consumed) VC and MBC were shown as a percentage of their predicted values, which were measured by the method of Baldwin, Richards, and Cournand[6]

$$\text{Respiratory reserve quotient} = \frac{\text{MBC} - \text{MV}}{\text{MBC}}$$

$$\text{Air velocity index (AVI)} = \frac{\text{Predicted MBC \%}}{\text{Predicted VC \%}}\ ^{20}$$

2. *Respiratory Gas Measurement.*—Measurement of residual volume (RV) was made by closed circuit[9] and open circuit methods.[11] Respiratory gas was estimated by using "Roken" gas analysis apparatus (Holden's modified analysis apparatus[37]) or Scholander's gas analyzer.[30]

Total lung capacity (TLC) : RV + VC.
Residual quotient: RV/TLC × 100.

Intrapulmonary gas mixing: nitrogen concentration in the alveolar air after rebreathing of pure oxygen for 7 minutes.

CO_2 content of alveolar air ($F_{A_{CO_2}}$) : analyzed from endexpiratory samples.

Partial pressure of CO_2 in expiratory gas ($P_{E_{CO_2}}$) and partial pressure of CO_2 in alveolar air ($P_{A_{CO_2}}$) : calculated from CO_2 content in expiratory gas ($F_{E_{CO_2}}$) and CO_2 content in alveolar gas ($F_{A_{CO_2}}$), respectively.

3. *Bronchospirometry.* Measurements were made by using Carlen's flexible double lumen catheter.[8]

Predicted value of the ratio of left to right was shown as the percentage of 46.5/53.5 in VC and of 46.8/53.2 in MBC.

4. *Blood Gas and pH Measurements.*—O_2 and CO_2 contents of arterial blood (Ca_{O_2} and Ca_{CO_2}) were estimated by Van Slyke-Neill's method,[38] and O_2 capacity was measured by Sendroy's method.[31] To estimate the pH of the blood, a glass-electrode[39] was used. Hematocrit (Ht) was measured by using Wintrobe's tube. O_2 saturation of arterial blood (Sa_{O_2}) was calculated from O_2 content and O_2 capacity. Partial pressure of O_2 in arterial blood (Pa_{O_2}), partial pressure of CO_2 in arterial blood (Pa_{CO_2}) and buffer base (Bb′) were computed from O_2 content, CO_2 content, pH of blood, and hematocrit by using Singer-Hasting's nomogram.[34]

5. *Derived Data.*—Oxygen partial pressure difference in millimeters of mercury between "alveolar air" and peripheral arterial blood ($P_{A_{O_2}} - Pa_{O_2}$) and the ratio of alveolar ventilation to pulmonary capillary blood flow ($\dot{V}_A/Qc$) were calculated by the next formula.[10, 26, 28]

$$\frac{\dot{V}_A}{Qc} = \frac{C\bar{v}_{CO_2} - Ca_{CO_2}}{F_{A_{CO_2}} \times 0.83}$$

$C\bar{v}_{CO_2}$: CO_2 content of mixed venous blood.

Dead space ratio: Volume of dead space (VD)/tidal volume (V_T).[10, 26, 28]

$$\frac{VD}{V_T} = \frac{Pa_{CO_2} - P_{E_{CO_2}}}{Pa_{CO_2}}$$

6. *Cardiac Catheterization.*—Both pulmonary arterial pressure and capillary pressure were estimated by an electromanometer, using a cardiac catheter, F. 8. Cardiac output (pulmonary blood flow) and cardiac index were measured by Fick's[18] and dye-dilution[17] methods.

For estimation of pulmonary circulation time, Evans blue dye was used. Arteriovenous O_2 differences were calculated from the O_2 content of arterial and mixed venous blood taken by catheter.

Pulmonary blood volume =

$$\frac{\text{Mean pulmonary circulation time} \times \text{Pulmonary blood flow}}{60}$$ [35]

Ventricular work against pressure =
$$\text{Cardiac output} \times \text{Pulmonary mean pressure} \times 0.1332$$ [27]

Pulmonary arteriolar resistance =
$$\frac{\text{Pulmonary mean pressure} - \text{Pulmonary capillary pressure}}{\text{Cardiac output}} \times 1332$$ [15]

Total pulmonary resistance =
$$\frac{\text{Pulmonary mean pressure}}{\text{Cardiac output}} \times 1332$$

RESULTS

These cases were classified into three groups according to the degree of anoxia and hypercapnia in arterial blood (Baldwin's classification of emphysema).[6]

Group I	Sa_{O_2}	more than 92% (after a standard exercise)
Group II	Sa_{O_2}	less than 92%,
	Pa_{CO_2}	less than 48 mm. Hg (after a standard exercise)
Group III	Sa_{O_2}	less than 92%,
	Pa_{CO_2}	more than 48 mm. Hg (after a standard exercise)

1. *Total Lung Capacity*.—When shown as a percentage of the predicted value, VC decreased in the order of the I, II, and III groups (Table II). Residual quotient increased, without relation to the degree of anoxia. TLC decreased even in Group I, and in Groups II and III further steady decrease was noted.

2. *Ventilation*.—Ventilation in liters per minute per square meter of body surface showed no great increase, exclusive of the first case, in which an increase was marked (Table II).

MBC decreased in proportion to the degree of emphysema. Although AVI decreased generally, it showed indefinite values. Respiratory reserve quotient decreased distinctively in Group III.

Although ventilatory equivalent showed indefinite values either at rest or under exercise, it decreased as a rule under exercise.

3. *Bronchospirometry*.—A percentage of its predicted value was expressed as in the ratio 46.5 : 53.5 of left to right. VC decreased on the affected side and MBC also decreased generally on the same side (Table III). MV decreased on the affected side, with one exception. O_2 consumption tended to lessen, except in 2 cases.

TABLE II

		GROUP										
		I		II							III	
CASE NO.		137	096	119	162	012	188	104	220	224	088	152
AGE (YEARS)		32	57	60	45	22	43	57	43	52	48	44
HEIGHT (CM.)		179	169	164	164	165	168	167	163	145	159	159
WEIGHT (Kg.)		53	52	41	55	44	45	51	57	43	44	44
SEX		M	M	M	M	M	M	M	M	M	M	M
Lung Volume												
Vital capacity (%)	B*	93	91	75	117	59	62	77	77	79	38	39
	A†	86	-	58	54	84	-	-	63	54	74	52
RV (%)	B	131	135	136	190	-	147	132	149	143	138	137
	A	245	-	217	158	210	-	-	143	199	201	282
TLC (%)	B	102	110	93	136	-	92	98	95	95	63	84
	A	123	-	108	80	115	-	-	84	90	106	110
$\frac{RV}{TLC} \times 100$	B	32	38	43	35	-	50	41	39	38	54	64
	A	47	-	62	49	45	-	-	45	55	47	64
Ventilation												
V_E (L./min./M.^{2})	B	6.8	4.3	3.8	3.7	-	4.1	3.9	5.4	4.7	4.5	5.1
	A	5.0	-	4.7	3.4	-	-	-	-	-	4.8	4.3
MBC (%)	B	90	76	50	68	22	54	85	81	77	36	24
	A	41	-	49	66	58	-	-	79	41	35	46
AVI	B	0.98	0.84	0.68	0.58	0.37	0.87	1.10	1.05	0.97	0.95	0.62
	A	0.48	-	0.85	1.22	0.69	-	-	1.25	0.77	0.49	0.88
RRQ‡ (%)	B	79	82	62	79	-	80	82	82	82	40	54
	A	66	-	79	85	88	-	-	85	73	50	68
VE§ Rest	B	4.8	3.6	4.5	2.9	-	2.3	4.2	4.0	3.2	2.9	3.3
	A	4.1	-	4.2	3.4	3.5	-	-	3.7	3.8	3.4	3.6
VE§ O_2	B	3.3	3.3	2.8	2.6	-	2.7	1.0	2.3	2.8	8.5	2.0
	A	4.2	-	1.7	2.1	1.5	-	-	3.3	3.9	3.3	2.0

*B = Before operation.
†A = After operation.
‡RRQ = Respiratory reserve quotient.
§VE = Respiratory equivalent.

TABLE III. BRONCHOSPIROMETRY

		GROUP															
		I		II										III			
CASE NO.		137		119		162		012		220		224		088		152	
AFFECTED SIDE (IN PARENS.)		r	(l)	(r)	l	(r)	l	(r)	l	(r)	l	r	(l)	(l)	l	(r)	l
VC (%)	B*	69.5	71.4	61.1	87.5	100.0	105.0	45.4	75.0	65.0	94.1	72.2	66.6	23.8	64.7	21.1	52.9
	A†	-	-	83.3	87.5	116.0	105.0	81.8	75.0	75.0	94.0	72.2	73.3	76.1	64.1	52.6	52.9
$\dot{V}_E$ (L./min.)	B	6.0	5.6	3.9	4.6	10.7	7.7	3.9	5.2	4.4	6.2	3.9	3.5	4.0	4.9	2.1	4.9
	A	-	-	5.6	5.9	10.7	7.7	6.8	8.2	5.6	6.4	4.4	3.9	8.6	3.3	5.0	3.3
MBC (%)	B	52.0	55.8	43.8	50.6	55.2	66.9	19.6	25.3	45.6	79.6	42.4	53.7	13.9	20.2	16.5	48.5
	A	-	-	51.8	51.2	62.4	66.9	38.4	42.2	51.2	79.3	43.6	57.8	68.1	56.9	28.1	30.7
$\dot{V}_{O_2}$ (c.c.)	B	460	390	132	287	132	332	250	370	210	110	196	130	110	201	190	220
	A	-	-	272	322	150	224	286	260	250	129	220	210	293	293	224	177

*B = Before operation.
†A = After operation.

TABLE IV

		GROUP																						
		I				II													III					
CASE NO.		096	137			012	104	119			162			188	224		220		088			152		
BEFORE-AFTER OPERATION		B*	B	2M†	10M	B	B	B	2M	9M	B	1M	6M	B	B	2M	B	2M	B	1M	4M	B	1M	6M
Sa_{O_2} (%)	Room air	93	93	94	95	94	87	92	93	94	90	95	95	89	89	91	89	93	84	91	92	86	94	94
	O_2	-	97	97	98	-	-	95	98	98	94	98	96	93	96	95	98	99	97	96	98	93	97	98
Pa_{O_2} (mm. Hg)	Room air	75	73	73	83	-	57	66	71	74	64	79	81	62	60	66	59	72	48	65	68	60	76	78
	O_2	-	116	115	119	-	-	81	113	131	77	109	91	74	98	79	126	137	100	93	123	76	103	113
Pa_{CO_2} (mm. Hg)	Room air	36	36	40	35	48	44	34	36	37	41	37	39	40	44	35	48	44	50	48	42	52	39	40
	O_2	-	36	41	36	-	-	35	39	40	41	39	38	40	44	36	48	44	49	52	45	49	43	38
pH (7.0)	Room air	.48	.38	.41	.40	-	.41	.43	.42	.40	.43	.42	.38	.38	.40	.40	.41	.40	.43	.39	.43	.37	.42	.41
	O_2	-	.38	.40	.39	-	-	.43	.40	.40	.38	.42	.38	.38	.40	.41	.40	.40	.43	.38	.41	.36	.39	.40
Bb (mEq. /L.)	Room air	44	44	46	44	-	49	47	45	45	45	45	46	44	51	42	48	49	53	49	50	45	48	46
	O_2	-	42	49	43	-	-	48	46	46	46	47	42	44	51	44	48	45	53	50	49	47	46	44
HCO_3^- (mEq. /L.)	Room air	22	21	24	21	-	27	23	23	24	24	23	22	24	29	21	27	27	31	28	28	26	25	25
	O_2	-	21	25	21	-	-	24	24	24	24	24	22	24	29	22	27	26	31	29	28	27	26	23

*B = Before operation.

†M = Months after operation.

4. *Index of Intrapulmonary Gas-Mixing.*—It has increased in all
without relation to the degree of emphysema.

5. *Arterial Blood.*—Sa_{O_2} at rest decreased in the order of the I, II
groups (Table IV). Improvement was seen, much more so than at 100
O_2 breathing, but never reached 100 per cent in all cases. Pa_{O_2} at rest
definitely, but it increased much more than that of 100 per cent O_2
time along with an increase of Sa_{O_2}. Pa_{CO_2} was within the normal lim
sive of that in Group III and it was not found to be increased more
time of 100 per cent O_2 breathing. pH was within the normal limits,
and HCO_3^- were above the normal value.

6. *Influence of Exercise.*—Minute volume per square meter of bod
increased 2 to 3 times under exercise (Table V). However, ventilator
lent decreased under exercise in most cases, although less marked.
Pa_{O_2} tended to decrease under exercise in all cases except 1, and sh
improvement even after 10 minutes. Pa_{CO_2} showed increase under exc
cases, but decreased in 3 cases, and in most cases recovery took place
minutes, although there was one exception in Group III in which ther
change. pH decreased under exercise in all cases, except 1 in Group III
there was a return to the value at rest after 30 minutes. Bb′ decreas
exercise in all cases as well as pH, but failed to return to the value at rest even after 10 minutes.

7. *Derived Data* (Table VI).—The physiologic dead space ratio increased. $P_{A_{O_2}} - Pa_{O_2}$ increased more than the normal value in all instances, while $\dot{V}_A/\dot{Q}c$ in most cases showed more than the normal value (0.8), namely, distribution-perfusion-relationship was abnormal.

8. *Pulmonary Circulation.*—Pulmonary arterial pressure rose more than the normal value in all cases as shown in Table VII, especially in 2 cases in Group III. Pulmonary capillary pressure was within the normal limits. Pulmonary blood flow, cardiac index, and stroke volume decreased distinctively in all cases. Arteriovenous difference of O_2 content decreased markedly more than the normal value. Pulmonary arterial resistance and total pulmonary resistance increased in general. Ventricular work against pressure decreased less than the normal value in all cases. Pulmonary blood volume decreased generally less than the normal value with a few exceptions. Mean pulmonary circulation time was prolonged longer than the normal value.

Re-examination of the postoperative cardiopulmonary dynamics 4 to 6 months later revealed the following results.

Postoperative Changes.—VC was decreased by thoracotomy in those patients who had presented normal values, but it increased in a case in Group III, in which there had been a marked decrease before operation. The residual quotient increased in most instances.

There were a number of cases in which TLC increased postoperatively although it had been decreased before the operation. This was particularly true

TABLE V

		GROUP																						
		I				II													III					
CASE NO.		96	137			12	104	119			162			188	220		224		88			152		
BEFORE-AFTER OPERATION		B*	B	2M†	10M	B	B	B	2M	9M	B	1M	6M	B	B	2M	B	2M	B	1M	4M	B	1M	6M
VE (L./min./M.)	Rest	4.8	6.8	5.0	5.1	-	3.9	3.8	4.7	3.7	3.7	4.5	3.4	4.1	5.4	-	4.7	-	4.4	5.7	4.8	5.1	5.5	4.3
	Exercise	12.0	12.8	23.2	14.0	-	14.3	11.7	13.0	12.7	13.7	-	9.5	11.8	-	-	9.8	-	7.9	10.3	11.1	14.5	12.1	10.7
VE‡	Rest	3.6	4.8	-	-	-	4.2	4.5	-	-	2.9	-	-	2.3	4.0	-	3.2	-	2.9	-	-	3.3	-	-
	Exercise	2.7	2.1	-	-	-	3.4	-	-	-	2.5	-	-	1.8	-	-	3.5	-	2.5	-	-	2.2	-	-
Sa_{O_2} %	Rest	93	93	94	95	94	87	92	93	94	90	95	95	89	89	93	89	91	84	91	92	86	94	96
	Exercise	-	88	87	89	-	82	83	87	86	82	95	89	90	80	84	87	91	72	83	78	80	75	89
	10 min. after ex.	-	96	92	89	-	86	85	82	96	77	92	92	88	82	84	87	91	75	83	91	72	88	93
Pa_{O_2} (mm. Hg)	Rest	75	73	73	83	-	57	66	69	74	64	79	81	62	59	72	60	66	48	65	68	86	94	96
	Exercise	-	65	56	62	-	49	51	59	55	49	82	59	68	46	50	57	73	41	49	46	80	75	89
	10 min. after ex.	-	55	58	63	-	54	52	47	59	41	71	62	60	48	50	57	69	45	44	66	72	88	93
Pa_{CO_2} (mm. Hg)	Rest	36	36	40	35	48	44	45	36	50	49	40	45	40	48	44	44	35	50	48	42	52	39	40
	Exercise	-	41	36	33	-	47	38	46	46	43	46	45	43	51	40	45	42	68	47	50	45	35	40
	10 min. after ex.	-	39	43	35	-	43	42	45	47	44	48	44	39	49	41	44	43	65	40	47	44	35	38
pH	Rest	7.40	7.38	7.41	7.40	-	7.41	7.43	7.42	7.40	7.43	7.38	7.38	7.38	7.41	7.40	7.40	7.40	7.43	7.39	7.43	7.37	7.43	7.41
	Exercise	-	7.28	7.39	7.39	-	7.35	7.35	7.32	7.38	7.37	7.40	7.40	7.33	7.38	7.39	7.38	7.31	7.26	7.38	7.35	7.35	7.42	7.36
	10 min. after ex.	-	7.38	7.38	7.39	-	7.39	7.39	7.39	7.43	7.42	7.41	7.41	7.37	7.39	7.39	7.39	7.35	7.25	7.45	7.37	7.40	7.44	7.39
Bb (mEq./L.)	Rest	44	44	46	44	-	49	47	45	46	45	46	45	44	48	49	51	42	53	48	50	45	48	46
	Exercise	-	39	44	42	-	46	42	42	43	42	44	43	42	47	46	51	40	47	48	48	45	45	43
	10 min. after ex.	-	43	47	43	-	49	45	43	45	44	46	43	43	47	47	50	42	47	50	46	45	45	44

*B = Before operation.
†M = Months after operation.
‡VE = Ventilatory equivalent.

TABLE VI

	GROUP																				
	I				II												III				
CASE NO	137			96	119			162			12	188	104	220		224		088			152		
BEFORE—AFTER OPERATION	2M	B*	10M†	B	B	2M	9M	B	1M	6M	B	B	B	B	2M	B	2M	B	1M	4M	B	1M	6M
VD/VT (%)	35	44	37	44	42	44	32	42	44	32	42	37	41	39	32	49	30	44	44	43	43	43	34
$P_{A_{O_2}}$—$P_{a_{O_2}}$ (mm Hg)	29	25	15	23	33	30	25	33	23	6	38	36	40	36	27	37	31	47	31	32	37	22	11
$\dot{V}_A/\dot{Q}_c$	1.2	0.9	—	—	1.0	1.0	—	0.8	0.8	—	—	1.0	1.0	1.1	1.0	1.2	1.0	1.6	1.3	—	1.2	1.1	—

*B = Before operation
†M = Months after operation

TABLE VII

	GROUP											
	I		II						III			
CASE NO	137		119		162		224		088		152	
BEFORE AFTER OPERATION	B*	A†	B	A	B	A	B	A	B	A	B	A
Pulmonary artery pressure (mm Hg)												
Systolic	22	27	24	25	22	15	32	27	45	38	30	31
Diastolic	10	6	11	5	10	5	18	12	17	12	17	7
Mean	17	16	16	13	15	10	23	17	26	20	20	17
Pulmonary capillary pressure (mm Hg)	12	8	11	4	6	5	7	8	5	12	7	5
Cardiac output (L/min)	3.08	3.81	2.76	4.16	2.54	3.07	2.90	3.60	3.87	7.55	2.67	3.20
Cardiac index (L/min/M²)	1.82	2.32	1.97	2.96	1.59	2.04	1.92	2.38	2.67	5.29	1.88	2.28
Stroke volume (c c/beat)	46	50	46	55	50	40	44	54	46	100	44	70
O_2 content of arterial blood (vol %)	19.14	18.75	16.78	13.91	16.79	18.67	21.38	19.48	17.38	14.73	13.01	12.46
O_2 saturation of arterial blood (%)	93.35	94.08	89.86	93.02	89.17	88.95	96.69	95.56	87.30	91.26	86.80	83.09
A V difference of O_2 content (vol %)	4.51	5.70	4.32	2.60	3.48	3.11	6.34	4.33	5.65	4.25	3.08	2.87
O_2 consumption (c c/min)	139	157	116	108	88	95	184	228	218	321	82	123
Pulmonary arteriolar resistance (dyne/sec/cm⁻⁵)	181	235	144	172	285	130	444	199	437	190	423	294
Total pulmonary resistance (dyne/sec/cm⁻⁵)	441	335	462	249	432	261	638	377	542	312	597	416
Right ventricular work (jouls/min)	6.7	6.5	5.7	12.5	4.6	5.6	8.9	8.1	13.1	28.1	6.7	7.2
Pulmonary blood volume (c c)	616	825	586	694	509	716	531	651	1032	1636	62	
Mean pulmonary circulation time (sec)	12.2	13.4	16.2	10.4	12.7	14.7	11.0	9.4	16.7	10.3	1	

*B = Before operation
†A = After operation

with the patients in Group III, who had a marked reduction preoperatively. Tidal volume was decreased in 1 patient, who once had shown an increase before operation, but the others showed no change. Although MBC, which had shown a marked preoperative decrease, increased in a few cases, in the majority there was a decrease after thoracotomy. The respiratory reserve quotient was increased in a number of cases, especially in those cases in which it had been low before the operation. Although, ventilatory equivalent was decreased in those cases in which there had been an increase before the operation, it was increased in those cases in which it had been decreased prior to the operation. Oxygen consumption was decreased in those cases which were above normal before the operation, but it had a tendency to increase in those cases which had been lower than normal.

Although intrapulmonary gas mixing was increased before the operation in all cases, it showed the normal value after the operation in most cases. Sa_{O_2} was improved in all cases, especially noticeable in those in which anoxia had been marked before the operation. Improvement of Pa_{O_2} was readily observed, even longer than 2 to 3 months. Pa_{CO_2} showed an indefinite value in those cases which had been within the normal limits, but it apparently decreased and indicated the normal value in those cases (No. 220, 88, and 152), in which there had been higher than normal values.

$P_{A_{O_2}} - Pa_{O_2}$ decreased gradually in all cases after the operation. V_D/V_T decreased in the cases in which there had been a marked increase. $\dot{V}_A/\dot{Q}_C$ decreased, getting near the normal value, i.e., 0.8, in all cases in which there had been an increase before the operation.

Postoperative measurement made 4 to 6 months afterward showed definite improvement of pulmonary arterial pressure which came close to the normal value. Pulmonary blood flow and cardiac index became higher. Arteriovenous O_2 difference and pulmonary arteriolar resistance, as well as total pulmonary resistance, decreased together, approaching the normal value. Ventricular work against pressure had a tendency to increase. There were a number of cases in which pulmonary circulation time decreased and returned to normal. Pulmonary blood volume increased generally, approaching the normal value.

DISCUSSION

Giant bullae with poor bronchial-bullous communication by their very nature cause considerable change in the capacity or ventilation of the lung, as shown by Baldwin,[6, 7] and Siebens,[32] and by us. This influence was further demonstrated by a return to normal respiratory function following removal of the bullae.

Although Baldwin[7] stated that hypoxemia which occurs with bullae was due to emphysema of the remaining lung, Siebens[32] reasoned that hypoxia was due to imbalance of alveolar ventilation and capillary blood flow to the remaining lung, which was affirmed by our results. However, as Baldwin and Siebens mentioned, in cases complicated with hypoxia and hypercapnia, emp the remaining lung may be the cause, which was confirmed by macros ings of the lung at the time of surgery and biopsy

Bullae seem to create a marked influence on the pulmonary circ evidenced by decreased pulmonary blood flow, increased total pulmon tance, and pulmonary hypertension

Our findings have been shown to be identical with those reporte Patrick,[21] except for pulmonary blood flow

Our animal experiments[13] have logically shown that altered p circulation does occur not only in the presence of the bullae but a presence of a balloon inserted into the pleural cavity of the animal, or conditions following extrapleural pneumothorax It is assumed that alteration develops whenever any pressure is exerted on the pulmonar

The fact that the resection of bullae relieves the characteristic physiologic cardiopulmonary change was well substantiated by our experimental and clinical results which agree with other reports

When, however, an advanced pulmonary emphysema accompanied the bullae formation, the situation is far more complicated It is most probable that the return of normal cardiopulmonary dynamics would be least expected despite resection of bullae Theoretically, the emphysematous condition would continue to exist

FitzPatrick reported that in the cases in which bullae were removed with poudrage there failed to be improvement in pulmonary arterial hypertension and total pulmonary resistance in certain instances Besides, hypoxia was not always improved

Since these results are to be expected, the rational treatment should be resection of the bullae with surgical treatment of the involved emphysema Crenshaw[11, 12, 13] and Abbott[1, 2, 3] have devised methods for the operative treatment of emphysema, which were aimed at pulmonary denervation with certain variations

According to his reports, Abbott[1, 2, 3] succeeded in obtaining improvement in symptoms and signs, and in lowering pulmonary arterial hypertension, while Crenshaw[11, 12, 13] was successful in relieving symptoms of advanced emphysematous patients who stood the operation well Postoperative improvement was definitely observed

The authors have attempted to resect bullae with incorporation of Crenshaw's operation in the cases in which hypoxemia and hypercapnia were present These patients improved despite a stormy postoperative course, and eventual remission occurred without fail as attested by lowering pulmonary arterial hypertension, with decreased total pulmonary resistance, thus differing from FitzPatrick's report The ratio between alveolar ventilation and pulmonary capillary blood flow became normal with correction of hypoxia and absence of hypercapnia

Baldwin[6, 7] and Siebens,[32] on the contrary, believed that the pulmonary bullae with advanced emphysematous complication should be retained, and that surgical intervention is contraindicated, because of the pulmonary physiology, and because respiratory insufficiency may ensue postoperatively.

Nevertheless, from our experience, emphysema, although advanced, should not necessarily be regarded as a contraindication, for various physiologic tests made after surgery have sufficiently proved the surgery to be legitimate. Therefore, the procedure of choice should be resection of the bullae with denervation for better cardiopulmonary dynamics with relief of symptoms and signs.

SUMMARY

Experiences with 11 cases of giant bullae are reported, in 8 of which resection and denervation were performed, resulting in definite postoperative improvement of symptoms and signs. The results obtained in pre- and postoperative physiologic investigation of the cardiopulmonary functions were:

1. Vital capacity was decreased markedly and residual volume was increased in the cases in which hypercapnia had been present. Gas mixing showed abnormal values in all cases. By means of bronchospirometry, vital capacity, minute volume, the maximum breathing capacity, and oxygen consumption were shown to be decreased on the affected side.

Sa_{O_2} and Pa_{O_2} were decreased, but Pa_{CO_2} increased in Group III. Physiologic dead space ratio and $PA_{O_2} - Pa_{O_2}$ were all increased, but there was definite decrease of pulmonary blood flow and cardiac index. Total pulmonary resistance was increased and pulmonary circulation time was prolonged.

2. Postoperatively, total lung capacity, gas mixing, Sa_{O_2}, Pa_{O_2}, $PA_{O_2} - Pa_{O_2}$, $\dot{V}A/\dot{Q}c$, pulmonary arterial pressure, pulmonary blood flow, total pulmonary resistance, and circulation time returned to normal values, respectively.

3. Since the abnormal physiologic cardiopulmonary findings in the presence of giant bullae are chiefly due to compression of the bullae on the remaining lung, operation is not contraindicated even if hypoxia is present.

Even in the cases in which giant bullae are complicated with emphysema and in which anoxia, hypercapnia, and pulmonary hypertension are present, normal pulmonary function can be obtained with surgical excision of the bullae, combined with denervation. In our opinion operation is not contraindicated in cases complicated with emphysema, but resection of the bullae with denervation is indicated.

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BRONCHOPULMONARY SEQUESTRATION

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BRONCHOPULMONARY SEQUESTRATION, at one time a subject of ir
to anatomists and embryologists alone, has within recent years
the interest of thoracic surgeons. The lesion is characterized by two
features, the cystic or bronchiectatic pulmonary disease and the syste
monary artery supplying the diseased lung. Thus its importance to the
surgeon is of necessity twofold. He is concerned with the preoperative
of the pulmonary lesion although it is usually only suspected rather than diagnosed. More important, however, is his concern with the operative recognition of the potentially dangerous vascular anomaly.

We have seen 7 patients with this anomaly at the State University of Iowa Hospitals in the past 5 years. Six of these were treated surgically and the seventh was discovered at the postmortem examination of a newborn infant.

PATHOLOGY

The pulmonary lesion is usually one of cystic or bronchiectatic disease of the lower lobe. More often than not the ectopic or sequestrated lung has no communication with the bronchial tree. Commonly, however, the adjacent basilar segments show bronchiectatic changes although they receive no anomalous blood supply. The lesions are usually on the left side and in our series were exclusively so. The cysts may be thin-walled, lined with cuboidal epithelium, or may resemble bronchiogenic cysts with pseudostratified columnar epithelial lining. The anomalous artery ordinarily arises from the lower thoracic aorta but may originate from the abdominal aorta or other abdominal arteries and traverse the diaphragm to reach the sequestrum.[4]

A distinction should be made between intralobar sequestration and extralobar sequestration (accessory lobe). The intralobar sequestrum is embedded in the lower lobe, usually in its posteromedial aspect and characteristically has venous drainage to the pulmonary vein. There is almost invariably an important element of infection. Accessory lobes are entirely separate from the lower lobe and may even be found beneath the diaphragm. There is little doubt, however, that this distinction between the two types may be made virtually impossible by the presence of chronic inflammatory changes binding the accessory lobe

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to surrounding normal lung. Venous drainage from accessory lobes is usually to the hemiazygos vein. Diaphragmatic defects are frequently associated with extralobar sequestration.[1, 3, 4, 12]

CLINICAL FINDINGS

Patients with this condition usually present themselves with histories of recurrent pulmonary infections. In the 8 cases reported by Pryce,[9] 7 of the patients had the onset of symptoms before they were 20 years of age. Our patients experienced a somewhat later onset of symptoms and 3 of the 7 had no symptoms referable to the pulmonary disease. Bronchoscopic examination is apt to show bronchial inflammation and purulent exudate in the lower lobe bronchus. Radiographic findings are not specific but recurrent inflammatory processes, cysts, or bronchiectasis limited to the left lower lobe should make one highly suspicious of pulmonary sequestration. We have not felt the need for angiographic proof of the diagnosis as proposed by Gerard and Lyons.[6]

ETIOLOGY

The cause of this peculiar combination of findings is still in doubt, although numerous theories have been advanced. The issue is clouded by the occurrence of each of the components (systemic pulmonary artery, cystic or bronchiectatic lung disease and, sometimes, diaphragmatic defects) separately.[3] It is nevertheless tempting to postulate some causal linkage between them when they do occur together. Pryce's[8, 9] approach to the problem, set forth so cogently in 1946 and 1947, has found many adherents and is probably the most widely quoted if not the most widely believed of all the applicable theories. Pryce believes that the systemic pulmonary artery, persisting in its fetal attachment to a portion of the lung, causes the ''captured'' bronchial bud to separate from the main pulmonary mass. This condition of ectopia is then apt to give rise to the pulmonary changes described previously.

R. A. Smith[10] states that an anomalous pulmonary artery is the primary lesion but suspects that the pulmonary changes are secondary to exposure to the relatively high systemic blood pressures.

Berman,[1] among others, believes that the pulmonary anomaly is primary and that the abnormal lung then attracts local independent blood supply from the most available source. Thus, structures having the characteristics of bronchogenic cysts, when they occur at the hilar level or above, are apt to have an independent blood supply from the pulmonary artery while similar structures near the medial aspects of the lower lobes are apt to be supplied by arteries arising from the nearby aorta.

Gebauer[5] carries this thought even further, stating that the primary pulmonary disease, usually acquired, stimulates the hypertrophy of vessels belonging to the ''network of the bronchial and mediastinal arteries'' and thereby takes the disease almost entirely out of the congenital class.

Boyden,[2] after carefully examining the theories of Pryce and Smith, concludes that ''a hypothesis of coincidental occurrence of these anomalies in certain patients is still all that can be warranted by the facts at our disposal.''

TREATMENT

Treatment consists of surgical excision of the diseased lung In extralobar sequestration, the sequestrum alone can be removed If the tion is of the intralobar type, a lobectomy or segmental resection of t segments is usually required Any accompanying diaphragmatic defect should be repaired Operative recognition of the lesion and its anomalous blood supply is essential The systemic pulmonary artery, usually found in the inferior pulmonary ligament, must be carefully dissected out and ligated Inadvertent cutting or tearing of this vessel may result in serious or even lethal hemorrhage [11]

CASE REPORTS

Summaries of the cases treated follow Some of the salient features are presented more succinctly in Table I

TABLE I

PATIENT	SEX	AGE	DURATION OF SYMPTOMS	BLOOD SUPPLY	INTRA OR EXTRA LOBAR	PATHOLOGY	BRONCHIAL COMMUNICATION
1 J B S	M	64	None	Through diaphragm	Extra	Pulmonary congestion and collapse, eventration of diaphragm	None
2 H B	M	32	1 yr	Aorta, 2 vessels	Intra	Advanced chronic inflammation	None
3 C W	M	56	2 yr	Aorta, 3 vessels	Intra	6 cm cyst and surrounding bronchiectasis	Yes
4 W C B	M	29	None	Aorta, 1 vessel	Intra	Cyst lined with bronchial epithelium, cellulitis of adjacent lung	None
5 R H	M	4	1 yr	Aorta, 1 vessel	Intra	Bronchiectasis and abscesses in basilar segments	Yes
6 D E	M	1 day	1 day	Aorta, 1 vessel	Extra	Atelectatic pulmonary tissue with fibrin in alveoli	No
7 L W	M	18	6 mo	Aorta, 1 vessel and pulmonary artery	Intra	Pneumonitis posterior basilar segment	No

CASE 1—J B S, a 64 year old white man, had no pulmonary symptoms but knew of a "lung cyst" demonstrated in chest roentgenograms 20 years previously He entered the hospital for treatment of an ulcer Radiographs revealed a radiolucent area in the left lower chest thought to be a lung cyst or a Bochdalek type diaphragmatic hernia (Fig 1, *A* and *B*) At surgery, a definite posterolateral diaphragmatic weakness was found There was also an extralobar sequestration which was removed and which showed congestion and pulmonary collapse microscopically The blood supply came through the diaphragm from a systemic artery

CASE 2.—H. B., a 32-year-old white man, had had two episodes of pneumonia in the previous year. Productive cough and dyspnea had followed the second of these which had occurred 6 months previously. Roentgenograms showed an irregular mass in the left lower lobe and bronchograms revealed minimal bronchiectasis of the basilar segments (Fig. 2, *A*, *B*, and *C*). Bronchoscopy showed purulent material coming from the left lower lobe. At the time of surgery an intralobar sequestrum showing advanced chronic inflammation was removed. Its blood supply consisted of two vessels arising from the lower thoracic aorta.

CASE 3.—C. W., a 56-year-old white man, had had pneumonia on the left side 2 years previously and had noticed a chronic cough since then. Roentgenograms of the chest revealed a cyst in the left lower lobe and bronchograms showed basilar bronchiectasis. A lower lobectomy was performed. Three arteries arising from the aorta supplied the cyst. The cyst had a bronchial communication and was lined with pseudostratified columnar epithelium.

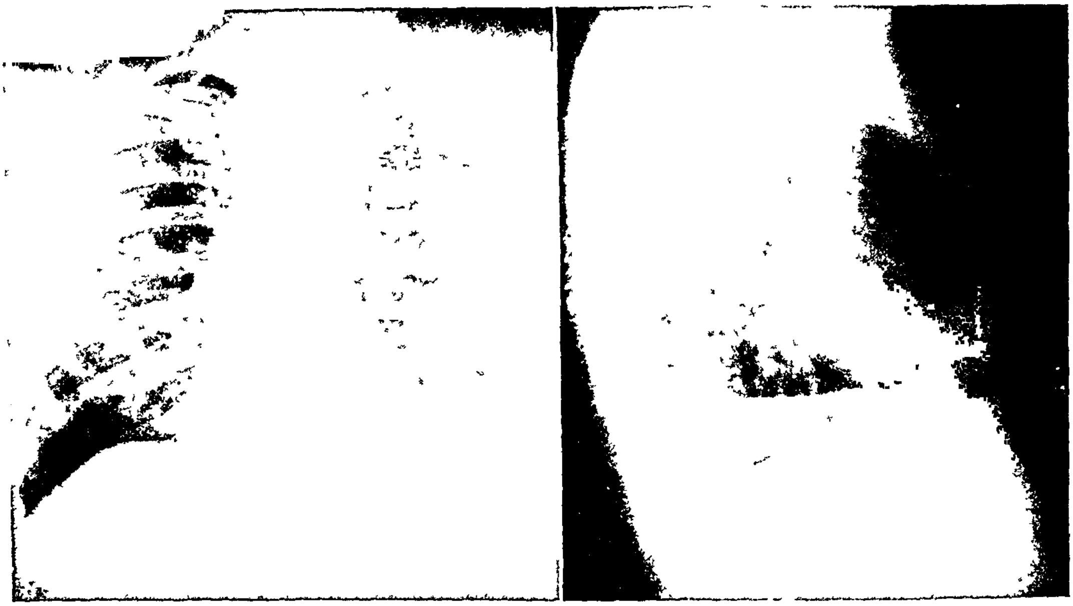
A *B*.

FIG. 1.—(Case 1.) *A* and *B*, Roentgenograms of the chest demonstrating the posterior diaphragmatic defect associated with the extrapulmonary sequestration.

CASE 4.—W. C. B., a 29 year-old white man, had no pulmonary symptoms but a left pulmonary shadow had been noted radiographically 1 month prior to admission. Bronchograms were normal as was bronchoscopy. A lower lobectomy was performed for a 7 cm. mass located posteriorly in the lower lobe. This mass was supplied by one artery coming from the aorta. It was lined with bronchial epithelium although there was no bronchial communication.

CASE 5.—R. H., a 4 year old white boy, had had repeated episodes of left lower lobe pneumonia during the previous year. Roentgenograms showed a left lower lobe shadow consistent with unresolved pneumonia (Fig. 3, *A* and *B*). An excision of the basilar segments was performed. They showed bronchiectasis with numerous abscesses. The anomalous vessel to these segments arose from the lower thoracic aorta.

CASE 6.—D. E. died on the first day of life from aspiration of vomitus. Besides congenital megacolon and bilateral partial ureteral obstruction, an extralobar sequestration or accessory lobe of the lung was found (Fig. 4).

CASE 7.—L. W., an 18 year old white man, had had left lower lobe pneumonia 6 months previously with persistent radiographic changes. Roentgenograms showed segmental atelectasis of the left lower lobe and bronchograms showed some clumping of the bronchi in this area.

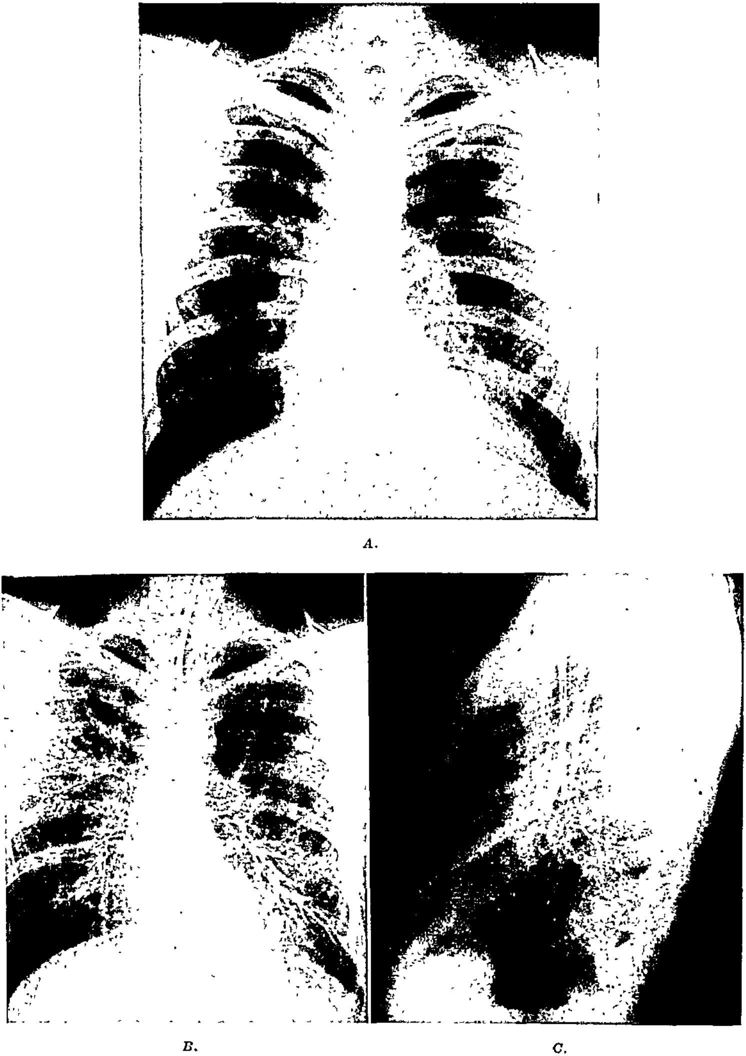

Fig. 2.—(Case 2.) *A* and *B*, Roentgenogram of the chest *(A)* and bronchograms *(B, C)* demonstrating the mass in the left lower lung field and the minimal amount of bronchiectasis in the lung tissue adjacent to it.

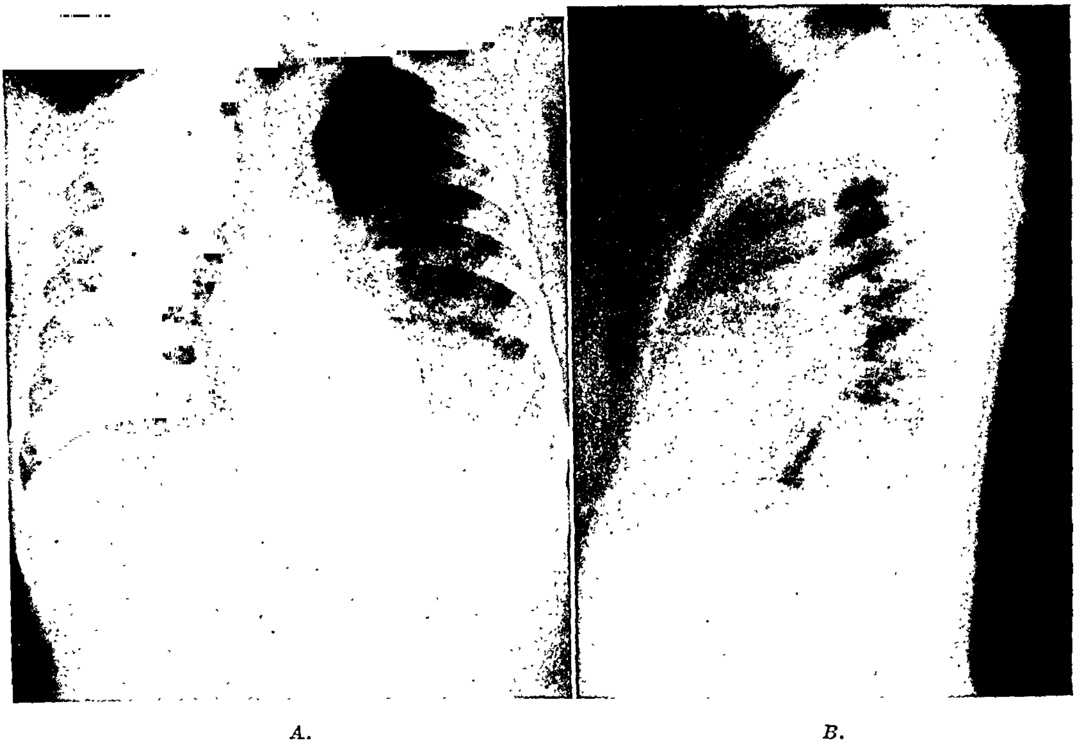

Fig. 3.—(Case 5.) *A* and *B*, Chest roentgenograms showing the infiltrate in the posterior basilar area of the left lower lobe.

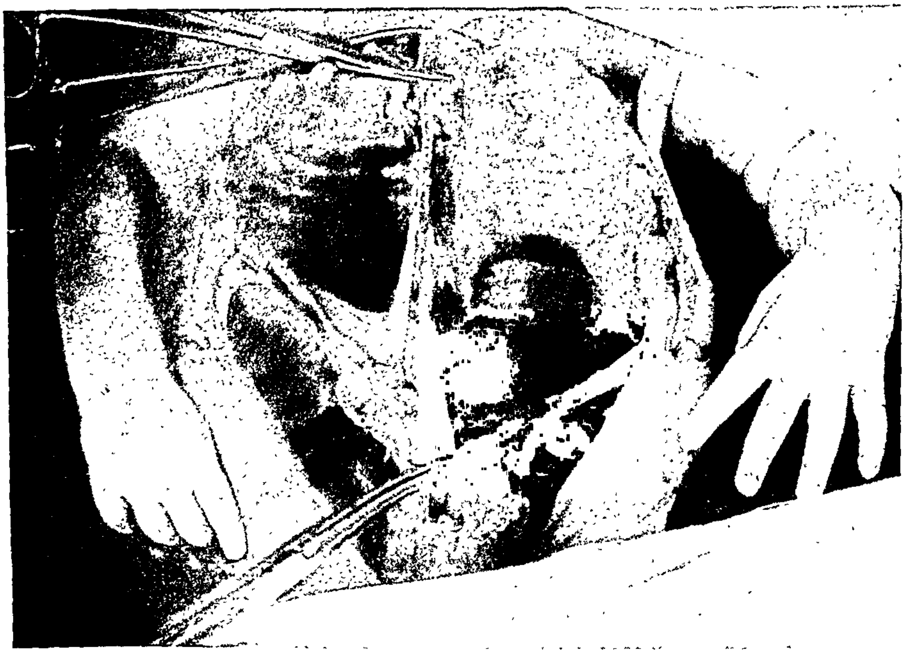

Fig. 4.—(Case 6.) Postmortem appearance of the extralobar pulmonary sequestration. Note the atelectatic accessory lobe and the vascular supply derived from the aorta. No bronchial communication could be demonstrated.

Bronchoscopy revealed bronchitis on the left, especially marked around the poster segment At surgery a mass in the posterior basilar segment, receiving its bl directly from the aorta, was found The basilar segments were resected Th chronic pneumonitis was supplied by both aortic and pulmonary branches but bronchial communication

DISCUSSION

Bronchopulmonary sequestration of the intralobar or extralobar types is usually asymptomatic lesion, but even when secondary infection or adjacent bronchiectasis does not call the patient's attention to the disease, a routine chest film probably will These facts as well as the medical profession's increasing awareness of surgical pulmonary diseases mean that larger numbers of these lesions will be seen by surgeons than have been in the past The surgeon treating these patients must be aware of the diagnostic possibility of bronchopulmonary sequestration whenever he sees a cystic or bronchiectatic lower lobe lesion, especially on the left side The value of suspecting or recognizing this anomaly lies largely in minimizing the danger of accidental injury to the anomalous vessel during the pulmonary surgery

SUMMARY

Seven cases of bronchopulmonary sequestration seen in the past 5 years have been described All of these were on the left side and in male patients The outstanding features of the disease in regard to clinical and pathologic findings and etiologic theories have been briefly reviewed

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DUODENOBRONCHIAL FISTULA

With a Summary of Abdominothoracic Fistulas

John L. Keeley, M.D., and Thomas A. Campbell, M.D., Chicago, Ill.

FISTULOUS CONNECTIONS between viscera are usually the result of ulceration, either benign or neoplastic, or secondary to gall stones. Such communications are usually between adjacent viscera. However, dissection and burrowing of an infectious, inflammatory, or ulcerative process may lead to the formation of a fistulous tract between widely separated structures either in the same body cavity or in adjacent ones. We wish to present a patient who had a duodenobronchial fistula. Despite a thorough search of the literature we have not encountered a report of a similar fistulous communication.

CASE REPORT

K. P., a 67-year-old man, was admitted to the West Side Veterans' Administration Hospital on June 27, 1955, because of a productive cough, weakness, and weight loss of 8 weeks' duration. His past history included a ruptured appendix in 1920 which was treated by drainage. Appendectomy was performed in 1922. One year later he had an episode of intestinal obstruction due to adhesions for which he was treated surgically. Another episode of intestinal obstruction occurred 6 years later, in 1929. In 1942, he underwent a cholecystostomy, but the details of his illness prior to this operation are unavailable. In 1950, he had been treated for pneumonitis at which time transitory hemoptysis was present.

During the month prior to his admission to the West Side Veterans' Hospital he had been hospitalized elsewhere, and a diagnosis of bronchiectasis had been made on the basis of x-ray and bronchoscopic findings. No evidence of tuberculosis or tumor had been demonstrated.

Physical examination disclosed an asthenic Negro man who appeared to be comfortable. The blood pressure was 118/70 mm. Hg. The heart was normal; there was a lag in respiratory movements of the chest. Resonance and breath sounds were decreased, and moist râles were scattered throughout the base of the right lung. There were three well-healed abdominal incisions resulting from his previous operations. The abdomen was otherwise normal as was the remainder of the physical examination.

The laboratory studies disclosed normal hemogram, serology, urinalysis, and electrocardiogram. Smears of gastric washings were negative for acid-fast bacilli on four occasions. The culture of the sputum revealed beta streptococcus and para-colon bacillus.

An x-ray study of the chest revealed diffuse mottling of the base of the right lung with slightly increased markings throughout the right lung field. There was displacement of the trachea and the heart to the right and some elevation of the diaphragm on the right (Fig. 1). These findings were considered compatible with the clinical diagnosis of bronchiectasis.

Bronchoscopy was negative except for the presence of purulent secretions in the segmental bronchi of the right lower lobe. The patient was treated for a time with

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Achromycin, Chlormycetin, and erythromycin with little benefit and without sputum. Following the studies thought pertinent to the productive cough, a more general investigation was begun.

Fluoroscopy following a barium meal disclosed a normal stomach and duodenal bulb. The junction of the first and second portions of the duodenum appeared to be retracted upward, laterally and posteriorly. From this point, barium escaped from the duodenal lumen into what was at first thought to be the common bile duct and its tributaries. However, films made following the fluoroscopy showed that the barium had entered the bronchial radicles in the right lower lobe. Roentgen ray studies in different projections demonstrated that a fistulous tract extended from the duodenum, passed posterior to the liver, traversed the diaphragm and entered the bronchial radicles of the posterior basal segment (Fig. 2). The second portion of the duodenum appeared to be smoothly compressed from the lateral side by an extrinsic mass. Intravenous cholecystography disclosed a distended gall bladder which was thought to account for the duodenal compression (Fig. 3).

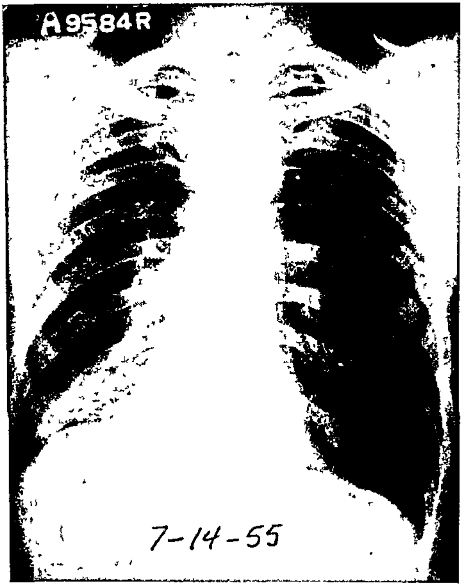

Fig. 1—Roentgenogram which shows diffuse mottling of the base of the right lung, some shift of the mediastinum to the right, and elevation of the diaphragm on the right. These findings were considered compatible with the clinical diagnosis of bronchiectasis

Attempts to pass a long tube beyond the fistulous tract and the distorted duodenum for feeding purposes and to decrease the contamination of the tracheobronchial tree were unsuccessful. It was thought that closure of the fistula would decrease the productive cough.

On Aug. 8, 1955, the abdomen was opened through a right subcostal incision and the fundus of the gall bladder was found to be firmly attached to the abdominal wall, presumably at the site of the previous cholecystostomy. There were dense adhesions between the gall bladder and the duodenum. The duodenum, a short distance from the pylorus,

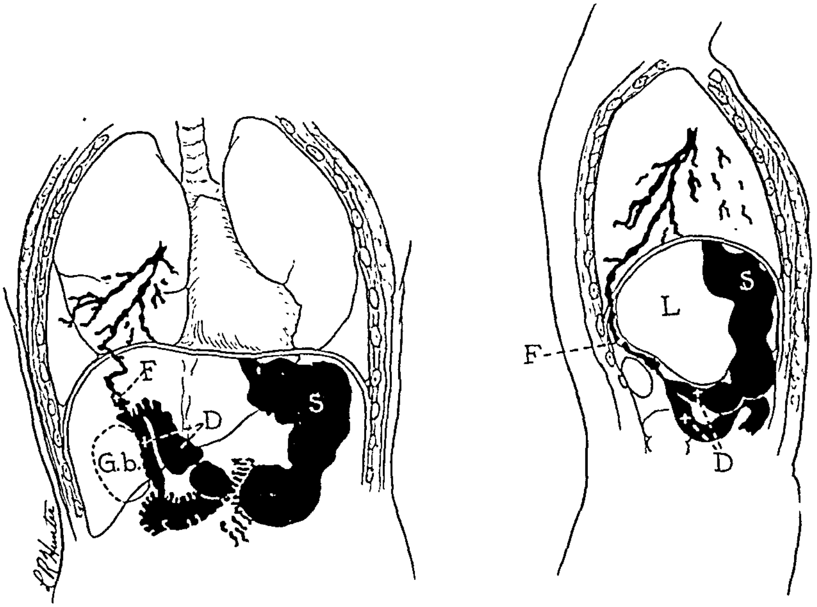

Fig. 2.—Tracings made from x-ray studies following a barium meal. The fistulous tract extended from the duodenum, passed posterior to the liver, traversed the diaphragm, and entered the bronchial radicles of the posterior segment of the lower lobe of the right lung.

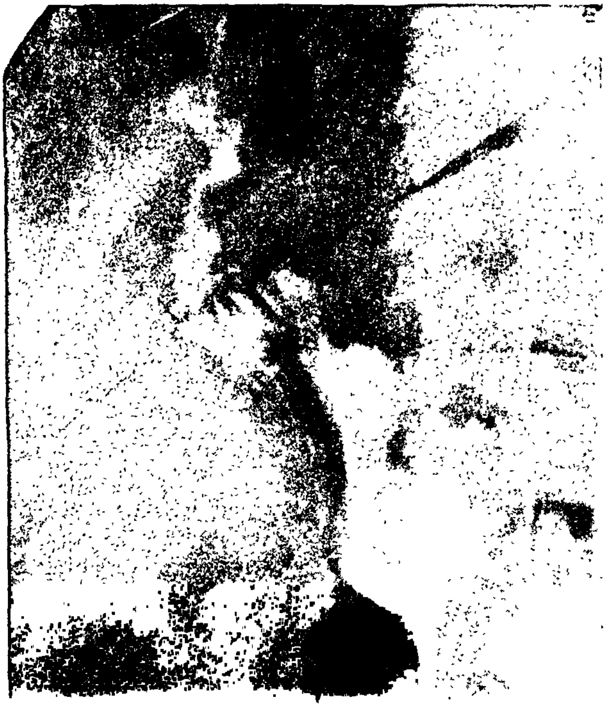

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Fig. 3.—Intravenous cholecystography showed the compression of the third portion of the duodenum to be due to a distended gall bladder.

was seen to pass posteriorly and superiorly to the region of the posterior subphrenic space. It then made a sharp angulation at its point of contact with the lower edge of the posterior surface of the liver. The second portion of the duodenum was identified passing in its usual direction. The foramen of Winslow was patent.

The junction between the first and second portions of the duodenum was separated from the undersurface of the liver and from a mass of scar tissue involving the posterior edge of the liver and the diaphragm The duodenum had an opening 1 cm in diameter on its free border. An opening of similar size was found in the mass of scar tissue.

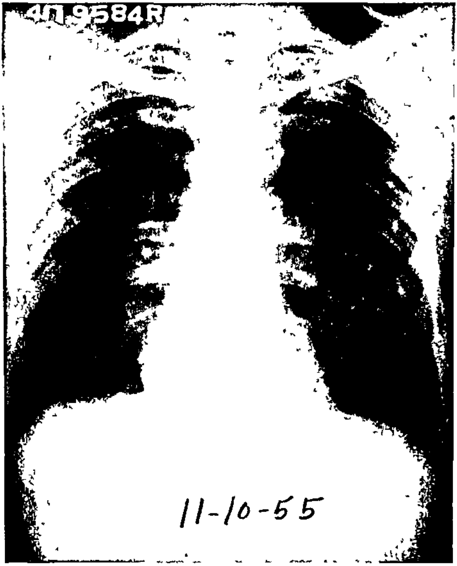

Fig. 4 —Roentgenogram of the chest made approximately 3 months after operation shows clearing of the lower lung field on the right, normal contour and level of the right diaphragm, and correction of mediastinal shift.

The duodenum revealed no other abnormality and no scarring, suggesting a chronic ulcer. The opening in the duodenum was closed with an inner row of catgut sutures and seromuscular sutures of cotton. The duodenum was displaced downward and wrapped in omentum to prevent the re-establishment of the fistula. A biopsy of the fistulous tract was taken. The gall bladder was removed. It was scarred and contained two stones, 1 cm. and 1.5 cm. in diameters. Suitable drains were put in place and the abdomen was closed.

The pathologic diagnosis was chronic cholecystitis and cholelithiasis and a fistulous tract with intestinal mucosa not further identified at the abdominal end. The early postoperative course was marked by episodes of chills and fever, and a white blood cell count of 48,000. By the fifth postoperative day, the temperature was normal and the white blood cell count was 14,000. The abdomen was soft, the Levine tube was removed and the patient received a liquid diet. A bronchogram on Aug. 26, 1955, failed to show any evidence of bronchiectasis of the middle or right lower lobes. A postoperative gastrointestinal study revealed less distortion of duodenum. Comparison of the preoperative and postoperative chest films showed considerable clearing in the right lower lung field (Fig. 4).

Following operation, the patient recovered rapidly. His cough subsided. He was dismissed from the hospital on Dec. 14, 1955, having been detained for completion of extensive dental care.

DISCUSSION

In the search for a previously recorded instance of duodenobronchial fistula, a variety of pathologic conditions below the diaphragm, which eventually communicated with the bronchial tree, were encountered. A summary of these widely scattered reports is offered.

It has, of course, been well established that subphrenic suppurative processes of long standing can eventually penetrate the diaphragm to cause empyema, pericarditis, pleurisy with effusion, or bronchial fistula. In the collective review of 3,608 patients with subphrenic abscesses, compiled by Ochsner and De Bakey,[1] 28.1 per cent had pleurisy or pleural effusion, 17.8 per cent had empyema, and 10.5 per cent had bronchopleural fistulas.

Hochberg's[2] series of 111 patients had a similar high incidence of these complications with 36 per cent, 19.2 per cent, and 4.7 per cent of pleurisy or pleurisy with effusion, empyema, and bronchopleural fistulas, respectively. Berens, Gray, and Dockerty[3] in reporting subphrenic abscesses in 154 patients, found pleural effusion in 54.5 per cent, empyema in 22.7 per cent, and bronchopleural fistulas in 11 per cent. The occurrence of bronchopleural fistula complicating subphrenic abscess appears to be well established.

Gullickson and Smith[4] have emphasized the desirability of immediate treatment for patients with subphrenic abscesses, who develop "bronchopleural-peritoneal" fistulas. They describe in detail 2 patients in whom rapid deterioration occurred following the establishment of this type of fistula and in whom bronchoscopic aspiration in one patient and tracheostomy and aspiration in the other appeared to be lifesaving.

Adams,[5] in discussing pleurobiliary and bronchobiliary fistulas, points out that most of these are associated with abdominothoracic war wounds and warns that if bile is found at thoracentesis, prompt drainage of the pleural space should be established. It is also urgent, he states, to establish adequate drainage in patients who cough up bile, as a fatal necrosing bronchitis may result from the action of bile plus secondary infection.

Adams reported 4 patients, 2 of whom developed empyema thoracis after rupture of a gangrenous gall bladder. Open drainage of the empyema cavity was done in both patients. Bile drained until appropriate biliary surgery was performed, after which the empyema healed. In the other 2 patients, a bronchobiliary fistula developed after cholecystectomy which was followed by jaundice. The eradication of common duct strictures in both of these patients was followed by the healing of the bronchobiliary fistulas.

Meyer,[6] in reporting the rupture of a pyogenic subphrenic abscess into the pericardium, emphasized the rarity of this occurrence. He also states that rupture of amebic liver abscess into the pericardium is rare, as it requires an abscess of the left lobe of the liver, an uncommon location. Gastric ulcers have ruptured into the pericardium. The use of antibiotics masks the symptoms of the original disease in many instances and may be responsible for delayed or missed diagnoses.

Neilsen, Dick, and Maddock (1950),[7] in reporting a perinephrobronchial fistula and psoas abscess with chronic perinephric infection, emphasize the insidious nature of perinephric infection and the great frequency of its late diagnosis. Their patient coughed up as much as two quarts of pus per day. Diagnoses of bronchiectasis and of carcinoma of the lung had previously been made. A mass developed in the right groin. Expectoration of large amounts of pus made the mass smaller. The cough stopped after the mass was drained of two quarts of pus. A urethral catheter was kept in the sinus in the right groin for 3 years. Healing occurred when it was removed.

Ribeiro (1939)[8] describes a patient who for 3 months had expectorated large quantities of foul sputum. Incision into a swelling in the left flank yielded 3 L. of pus. The foul expectoration persisted, as did a fistula in the incision. Roentgenograms showed a voluminous calculus in the region of the left kidney. At the second operation it was removed in pieces and a nephrectomy was done. As the upper pole of the kidney was being freed from the diaphragm, a "lumbobronchial" fistula was found. The patient was under spinal anesthesia and began to cough bloody mucopurulent material. Cough and expectoration stopped 8 days later. The fistula in the flank persisted and opaque media injected into it entered what appeared to be small bowel, as judged by the mucosal pattern. Curetting and packing the fistula was followed by healing. It is possible that a loop of small bowel had become adherent to the infected kidney and that the fistula occurred at this point.

Urizza and Gama,[9] in 1954, reported a patient with hemoptysis and, later, mucopurulent sputum. Following a barium meal, he expectorated barium, and a diagnosis of gastrobronchial fistula was made. His complete preoperative diagnosis was diaphragmatic hernia, gastrobronchial fistula, and bronchiectasis of the left lower lobe or lingula. At operation an "anterior" diaphragmatic hernia was found. A fistula had developed between the intrathoracic portion of the stomach and the tip of the lingula. A partial gastric resection was done to remove the area of the fistulous opening. The hernia was repaired, and a lingulectomy was performed. Microscopic examination of the lingula disclosed atelectasis, fibrosis, cystic bronchiectasis, nonspecific bronchial infection, and lipoid pneumonia. The patient made a prompt recovery and was ambulatory after the fourth postoperative day.

We are unable to prove the sequence of events which led to the formation of the fistula in our patient. He was well for 6 years after drainage of the gall bladder; therefore, injury to the duodenum during the operation is not considered responsible. Then an episode of "pneumonitis with hemoptysis" occurred. However, it was not until 5 years later that bronchiectasis was diagnosed. At the operation for the bronchoduodenal fistula there appeared to be no findings suggesting serious gall bladder disease, such as gangrene or continuing fibrosis. There was no evidence of malignant disease.

We are left with two reasonable possibilities. One is the perforation of a duodenal diverticulum. This appears to be rather unlikely as they are usually

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COCCIDIOIDOMA

Charles E. Owens, M.D., George A. Paulsen, M.D., and Jack Dykes, M.D., Bakersfield, Calif.*

COCCIDIOIDOMA is a lesion which is endemic to the southwestern part of the United States. Thus, in most collective series of pulmonary granulomas, the fungus *Coccidioides immitis* is rarely isolated as the causative agent. The lack of familiarity with this lesion has led many clinicians to picture the coccidioidoma as a solid granuloma without a virulent potential. That such lesions are not generally solid nor sterile is well borne out by the following presentation of patients. The chest x-ray studies and gross pathologic findings are illustrated by the accompanying photographs of a typical case (Figs. 1 and 2).

MATERIALS AND METHODS

During the 10-year period from 1948 to 1958, 25 cases of coccidioidoma were treated surgically on the County and private thoracic surgical services in Bakersfield, California. On initial x-ray examination these cases met the following criteria: (1) location in the substance of the lung, (2) no apparent cavitation, (3) absence of obstructive changes in the lung peripheral to the lesion, and (4) no other significant pathological change in the lung fields. The causative organism was observed in every case, on the wet mount preparation, in the stained sections, or by culture.

OBSERVATIONS

There were 22 Caucasians, 2 Negroes, and 1 Filipino involved in this series. The lesion was found in 13 males and 12 females with the age range evenly distributed between 20 and 60 years of age for both sexes (Table I).

TABLE I. AGE AND SEX

	AGE (YEARS)							
	–20	21-30	31-40	41-50	51-60	61-70	71-80	TOTAL
Male	1	2	2	3	3	1	1	13
Female		3	4	2	2	1		12
Totals	1	5	6	5	5	2	1	25

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No acute or pneumonic history was elicited in 12 patients, the lesion being letected on a survey chest roentgenogram (Table II). In those 13 patients resenting symptoms, the interval between x-ray findings and surgery was less han 3 months in 5 patients and over 12 months in 8. The latter group illusrates the tendency to observe these lesions for extended periods of time in cerain cases.

TABLE II. CLINICAL HISTORY

	INTERVAL BETWEEN X RAY FINDING AND SURGERY	
	UNDER 3 MO.	12 MO. AND OVER
Symptoms prompting x ray	5	8
Asymptomatic: routine film	12	

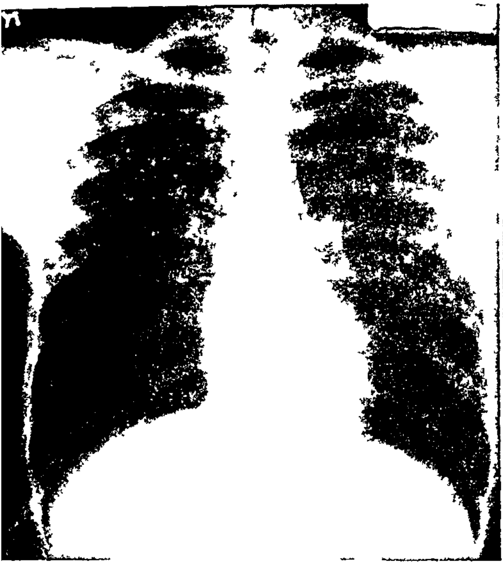

Fig 1

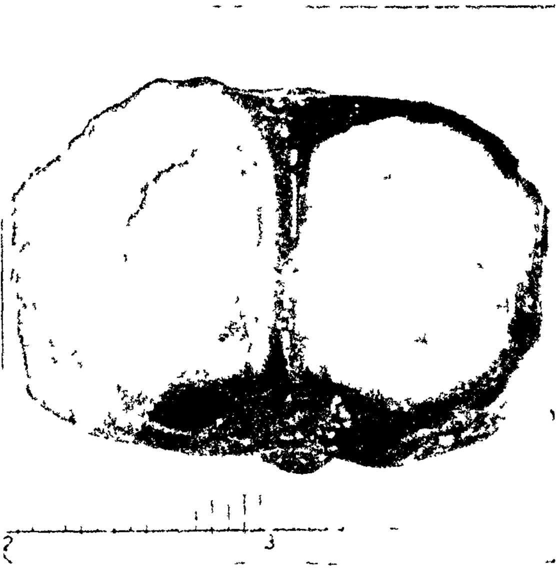

Fig 2

Fig 1—Posteroanterior roentgenogram of the chest in a 21-year-old man Note the coccidioidoma in the right upper lobe

Fig 2—Photograph of gross specimen disclosed in Fig 1

Skin tests for coccidioidomycosis were done presurgically on 18 patients, and in 11 of them the reaction was positive. Positive tuberculin reactions were obtained in 6 of 15 patients tested. Five symptomatic patients exhibited negative coccidioidin skin tests at the time of surgery. Retesting a number of weeks later might have shown a conversion to a positive reaction, but the possibility of malignancy precluded such a waiting period in some cases. Positive precipitin and complement fixation titers were obtained in 2 and 4 cases, respectively, out of 16 cases tested (Table III).

TABLE III. SEROLOGY

	16 CASES TESTED	
	POSITIVE	NO REACTION
Precipitin titer	2	14
Complement fixation	4	12

The indications for surgery fall into two principal groups: (1) a round lesion in which the possibility of malignancy cannot be ruled out, and (2) a radiodensity which intermittently cavitates.

The peripheral location of the coccidioidoma makes bronchoscopy, node biopsies, and cytologic studies of the sputum unrewarding in making a diagnosis as in other peripherally located tumors. The intermittently cavitating granuloma must be considered as a possible source of seeding of other areas of the pulmonary parenchyma. That such contamination does take place is suggested by 1 case in this series.

Preoperative chest x-ray studies were inconclusive in ascertaining the etiology of the solitary lesion until, as occurred in 6 cases, the onset of radiolucency or air-fluid levels. In the remaining 19 cases, the absence of calcium made carcinoma at least suspect in every case. However, microscopic examination of the surgical specimen did reveal scattered central calcification in 4 cases. The significant finding of lamination which is considered pathognomonic for granulomas was not observed in roentgenograms and fibrous lamination was seen grossly in only 2 cases.

The anatomic location of the coccidioidoma showed equal distribution between the upper and lower lobes, the right lower lobe and the left upper lobe containing 15 of the 25 lesions. Previous work emphasized the tendency for occurrence near the lower and mid-lung fields. It would seem there is no actual lobe preference.

The gross size of the granulomas varied from 1.2 cm. to 4 cm., with the average diameter of all lesions being 2.4 cm. (Table IV).

TABLE IV. GROSS SIZE OF LESION

	SIZE (CENTIMETERS)*						
	UNDER 1 CM.	1.0-1.5	1.6-2.0	2.1-2.5	2.6-3.0	3.1-3.5	3.6-4.0
Number of cases	0	2	8	5	5	3	2

*X-ray measurement larger.

The gross pathology was uniform. All of the coccidioidomas exhibited a fibrous capsule varying from 1 to 4 mm. in width, and in all there was central necrosis or caseation (Table V). As mentioned previously, two nodules contained fibrous lamination.

TABLE V. GROSS PATHOLOGY

Fibrous capsule	25 cases
Central necrosis	25 cases
Solid granuloma	0 cases
Lamination present	2 cases

The difficulty of obtaining a specific diagnosis in a granulomatous lesion is well known to the thoracic surgeon. The methods used in this series are tabulated in Table VI. The occasional discovery of coccidioidal spherules in the wet mount, when all other methods are negative, illustrates the problem of causative organism identification. Also of interest is the 1 case of a positive culture on material taken from the surgical specimen, yet the wet mount and stained sections failed to disclose the organism. Unless all available means of organism detection are utilized, the diagnosis of nonspecific granuloma will be a common one.

TABLE VI. DETECTION OF COCCIDIOIDAL ORGANISM IN ALL 25 CASES

Wet mount preparation	14	Positive Coccidioides culture on sputum	1
Permanent surg. section:		Culture on surgical specimen	2
A. Spherules	19	Positive wet mount with negative microscopic	2
B. Mycelia	4		
Spherules in sputum	1	Negative wet mount, negative microscopic with positive culture	1

In 3 patients, postoperative difficulties occurred. Two of the problems were atelectasis and both were cleared by bronchoscopy. The third complication was venous thrombosis of the lower extremities.

EXTENT OF RESECTION

Surgery performed here for coccidioidoma is usually of a segmental or subsegmental nature, as is implied by their location and average diameter of approximately 2.5 cm. (Table VII). On occasion, a lobe or more must be resected because of chronic inflammation or a hilar position. The extent of resection in coccidioidal granuloma and cavitation has been much discussed in regard to recurrent disease and postoperative complications. Satellite nodules have been held responsible for postoperative empyema and pulmonary dissemination of the fungus or recurrent cavitation. Some thoracic surgeons thus perform lobectomy as the minimal procedure. In our series, partial lobectomy was done in 17 out of 25 cases, and in none of these did postoperative difficulties occur which were related to the organism. In the 1 case requiring pneumonectomy, the lesion initially presented as a solid granuloma and then progressed to the stage of multiple cavities. A lesser procedure was not feasible at the time of surgery since a large cavity involved almost the entire left upper lobe and a smaller cavity was intimately adherent to the vascular supply to the lower lobe.

TABLE VII. EXTENT OF PULMONARY RESECTION

Subsegmental lobectomy (wedge)	13 cases
Segmental lobectomy	4 cases
Lobectomy	7 cases
Pneumonectomy	1 case

DISCUSSION

There is general agreement that an undiagnosed solitary pulmonary nodule deserves excision, and a large number of coccidioidomas are removed for suspected malignancy. Most reports of so-called coin lesions list malignancy as the etiology in some 20 to 35 per cent of cases In an endemic area, such as the San Joaquin Valley of California, malignancy is found in a much smaller percentage The coccidioidin skin test is not an effective differential tool, since most residents of this area have a positive reaction Likewise, the coccidioidal serologic findings are of little value, since in most cases of chronic granuloma the host immune response has resolved to levels that cannot be detected

In those cases in which coccidioidomycosis is the presumptive preoperative diagnosis, the surgical indications largely relate to persistent cavitation and its accompanying symptoms Some physicians regard both coccidioidal cavitation and coccidioidomas as asymptomatic lesions rarely requiring surgery While it is undoubtedly true that there are many undiagnosed asymptomatic granulomas, it is of interest that 13 of the 25 patients in this series were seen because of persistent respiratory symptoms

The epidemiology of the coccidioidoma is important in evaluating the surgical indications for its removal That viable organisms are present in the granuloma wall in both spherule and/or mycelia form is a fact, yet man to man transmission of the disease or later extrapulmonary dissemination from a pulmonary focus has never been proved More likely is the possibility of endobronchial spread of the fungus as a process of shelling occurs In such a situation the inoculating dose could be large enough to set up a new site of pulmonary disease in spite of the patient's immune response Cavitation at secondary sites in the presence of granuloma has been reported by others and was found in 1 case in this series Another explanation of the later appearance of cavitation could be that undetected foci of fungal infection were present in the lung and became detectable with renewed activity In any case, they attest to the spreading potentialities of the organism in nondisseminated cases of pulmonary lesions

SUMMARY

Twenty five cases of coccidioidoma are presented, in all of which the fungus has been recovered in the surgical specimen Twelve of the patients were asymptomatic, while 13 initially presented symptoms The principal surgical indications were the possibility of malignancy and recurrent cavitation Skin tests, coccidioidal serology, and chest x ray studies were of limited positive value in making a specific diagnosis The gross pathologic findings are stressed, there being central necrosis with a fibrous capsule in all lesions Surgery consisted of partial lobectomy in most cases, and there has been no apparent spread or recurrent disease in these cases

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THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

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Program

MEMORANDA FOR GUIDANCE OF SPEAKERS

1 In accordance with the By Laws of the Association, the papers which are read at the meeting shall be given to the Reporter *immediately after presentation* If these papers are not submitted promptly their publication may be delayed

2 In publication it is customary to group discussions together on a series of papers Any delay in the return of corrected discussions to the Editor means that publication of all papers on the subject will be held up This is manifestly unfair to those who are conscientious in the prompt submission of their remarks for publication Undue tardiness may mean that the discussion will not be published

3 *Regular Program* Speakers will be limited to 15 minutes

4 *Thoracic Surgery Forum* Speakers will be limited to 10 minutes Papers on the Thoracic Surgery forum as submitted for publication will be limited to 3,000 words At the discretion of the President, limited discussion will be allowed following the formal presentations

5 *Discussion of Papers* Discussers will be limited to 3 minutes Only members of the Association and invited speakers will have the privilege of discussing papers

Wednesday Morning, May 11, 1960

8 30 A M Business Meeting (Limited to Members)
Napoleon Room

8 45 A M Scientific Session REGULAR PROGRAM
Napoleon Room

1 **The Use of Direct Myocardial Stimulating Electrodes in Complete Atrioventricular Block** Bernard S Levowitz (by invitation), William B Ford, and James W Smith, Jr (by invitation), Pittsburgh, Pa

2 **Surgical Correction of Transposition of the Great Vessels A Five Year Survey** Thomas G Baffes, Maurice Lev (by invitation), Milton H Paul (by invitation), Robert A Miller (by invitation), William L Riker (by invitation), Arthur DeBoer (by invitation), and Willis J Potts, Chicago, Ill

3 **Surgical Palliation in Patients With Ebstein's Anomaly and Congenital Hypoplasia of the Right Ventricle** Milton Weinberg, Jr (by invitation), Juan P Bicoff (by invitation), Lawrence Luan (by invitation), Zwi Steiger (by invitation), Benjamin M Gasul (by invitation), and Egbert H. Fell, Chicago, Ill

4 **Myocardial Infarction in Infancy The Surgical Management of a Complication of Congenital Origin of the Left Coronary Artery From the Pulmonary Artery** David C Sabiston, Jr, Salvatore Pelargonio (by invitation), and Helen B Taussig (by invitation), Baltimore, Md

5. **Diagnosis and Surgical Treatment of Intracardiac Myxoma and Rhabdomyoma.** Rodman E. Taber and Conrad R. Lam, Detroit, Mich.
6. **Vasomotor Activity During Total Body Perfusion.** Paul W. Sanger, Frederick H. Taylor, and Francis Robicsek (by invitation), Charlotte, N. C.

Wednesday Afternoon, May 11, 1960

2:00 P.M. Scientific Session: REGULAR PROGRAM
Napoleon Room

7. **Studies of Peripheral Vascular Resistance Associated With Total Cardiopulmonary Bypass. I. Peripheral Resistance Under Condition of Normothermia and Normotension.** A. Robert Cordell (by invitation), Merrill P. Spencer (by invitation), and Jesse H. Meredith (by invitation), Winston-Salem, N. C.
8. **Lipuria and Lipasemia After Thoracic Surgical Procedures.** F. Price Cossman (by invitation), Federico Adler (by invitation), and C. Frederick Kittle, Kansas City, Kans.
9. **Analysis of Fifty Cases of Pulmonary Emphysema, Blebs, and Bullae Treated Surgically.** Jerome R. Head, Theodore R. Hudson, Louis R. Head (by invitation), and James M. Head (by invitation), Chicago, Ill.
10. **Lung Abscess in Japan.** Kingo Shinoi (by invitation), Tokyo, Japan.
11. **A Study of Essential Hemoptysis.** Raymond J. Barrett and William M. Tuttle, Detroit, Mich.
12. **Ligation and Division of the Bronchus in the Surgical Treatment of Cavitary Tuberculosis.** J. Maxwell Chamberlain and Thomas M. McNeill (by invitation), New York, N. Y.
13. **The Culture of Tubercle Bacilli from Resected Specimens of "So-called" Negative Patients.** William P. Coghlan (by invitation), George S. Willauer, Charles Fineberg (by invitation), and Robert G. Johnson (by invitation), Philadelphia, Pa.

Thursday Morning, May 12, 1960

8:30 A.M. Scientific Session: THORACIC SURGERY FORUM
Napoleon Room

14. **The Subcoronary Implantation of a Flexible Tricuspid Aortic Valve Prosthesis.** Benson B. Roe, Mervyn F. Burke (by invitation), and Harry Zehner (by invitation), San Francisco, Calif.
15. **Experimental Production of Aortic Stenosis.** Anthony J. Munoz (by invitation), and Sam E. Stephenson, Jr. (by invitation), Nashville, Tenn.
16. **Evaluation of a New Nonwettable Macroporous Membrane With High Permeability Constants for Possible Use in a Membrane Oxygenator.** James S. McCaughan (by invitation), Richard Weeder (by invitation), John C. Schuder (by invitation), and William S. Blakemore, Philadelphia, Pa.
17. **Temperature Compensated, Self-Calibrated Oxygen Monitoring Device.** Jesse H. Meredith (by invitation), John H. Artesani (by invitation), and Joseph Mamlin (by invitation), Winston-Salem, N. C.
18. **Pulmonary Arterial Hypoxia Versus Inspiratory Hypoxia in Relation to Increased Pulmonary Vascular Resistance.** Peter V. Moulder, Joseph Lancaster (by invitation), Robert W. Harrison (by invitation), Stephen Michel (by invitation), and Richard G. Thompson (by invitation), Chicago, Ill.
19. **Treatment of Bank Blood by Resins.** Edward D. McLaughlin (by invitation), Thomas F. Nealon, Jr., and John H. Gibbon, Jr., Philadelphia, Pa.

20 **Gas Exchange Dynamics of Glycerolized Frozen Blood** Thomas G O'Brien (by invitation), Chelsea, Mass, and Elton Watkins, Jr, Boston, Mass

21 **The Relationship of the Sympatho Adrenal System to Potassium Flux and Cardiac Irritability Induced by Alterations in Blood pH** Bernard Goott (by invitation), J Rosenberg (by invitation), R C Lillehei (by invitation), Fletcher A Miller (by invitation), and Owen H Wangensteen, Minneapolis, Minn

22 **Bronchoscopy and Bacteremia** Sheldon Oscar Burman (by invitation), Pittsburgh, Pa

23 **Altered Hemodynamics in the Pulmonary Circulation Following Reaeration of an Atelectatic Lung** Edwin Tutt Long (by invitation), Arthur F Reimann (by invitation) Takamaru Mikouchi (by invitation), John R Benfield (by invitation), and Salvatore L Nigro (by invitation), Chicago, Ill

24 **Selective Chemotherapy of the Lung During Unilateral Pulmonary Arterial Occlusion With a Balloon Tipped Catheter** Nicholas P D Smyth (by invitation), and Brian Blades, Washington, D C

25 **An Experimental Study of Pulmonary Artery Replacement** Joseph W Gilbert, Jr (by invitation), William P Cornell (by invitation), and Theodore Cooper (by invitation), Bethesda, Md

26 **A Simple Device for the Mechanical Anastomosis of Blood Vessels** Timothy Takaro, Oteen, N C

27 **Experimental Left Coronary Artery Perfusion Through an Aortotomy During Cardiopulmonary Bypass** James B Littlefield (by invitation), Edward M Lowicki (by invitation), and William H Muller, Jr, Charlottesville, Va

28 **Growth of Cardiovascular Chambers Following Cardiac and Aortic Surgery** Sigmund A Wesolowski (by invitation), Lester R Sauvage (by invitation), Philip N Sawyer (by invitation), and Karl E Karlson, Brooklyn, N Y

Thursday Afternoon, May 12, 1960

2 00 P M Executive Session (Limited to Active and Senior Members)
Napoleon Room

3 00 P M Scientific Session REGULAR PROGRAM
Napoleon Room
Address by the President, William E Adams, Chicago, Ill
Address by Honored Guest, Alfonso Topete, Chairman, Department of Surgery, University of Guadalajara, Mexico **New Findings in the Coronary Encephalic Perfusion in Depressive Surgical Cases**

29 **Coarctation of the Aorta With Particular Emphasis Upon Improved Techniques of Surgical Repair** George C Morris, Jr (by invitation), Denton A Cooley, Michael E De Bakey and E Stanley Crawford, Houston, Tex

7 00 P M Banquet and Dancing, Casanova Room
Attendance limited to Members of the Association and their ladies, Invited Speakers and their ladies
Dinner dress preferred

Friday Morning, May 13, 1960

9 00 A M Scientific Session REGULAR PROGRAM
Napoleon Room

30 **A Five Year Follow up Study of Closed Mitral Valvulotomy** J Gordon Scannell, John F Burke (by invitation), and Farrokh Saidi (by invitation), Boston, Mass

31. **Valvuloplasty for Acquired Aortic Stenosis.** Donald G. Mulder (by invitation), Albert A. Kattus (by invitation), and William P. Longmire, Jr., Los Angeles, Calif.
32. **Partial and Complete Aortic Valve Prostheses in Advanced Aortic Insufficiency.** Dwight E. Harken, Warren J. Taylor (by invitation), Harry S. Soroff (by invitation), Armand A. Lefemine (by invitation), Sushil K. Gupta (by invitation), and Steven Lunzer (by invitation), Boston, Mass.
33. **The Results of Surgical Treatment for Ventricular Septal Defect.** John W. Kirklin, Dwight C. McGoon, and James W. DuShane (by invitation), Rochester, Minn.
34. **The Closure of Atrial Septal Defects Utilizing General Hypothermia: The Effectiveness of Treatment as Determined by Cardiac Catheterization.** Andrew G. Morrow, Joseph W. Gilbert, Jr. (by invitation), R. Robinson Baker (by invitation), and N. Perryman Collins (by invitation), Bethesda, Md.
35. **Elective Cardiac Arrest Using Selective Cardiac Hypothermia.** David M. Long, Jr. (by invitation), Laurence P. Sterns (by invitation), Vincent L. Gott (by invitation), Robert H. DeRiemer (by invitation), and C. Walton Lillehei, Minneapolis, Minn.
36. **Open Heart Surgery Using Deep Hypothermia Without an Oxygenator.** Archer S. Gordon (by invitation), Bertrand W. Meyer, and John C. Jones, Los Angeles, Calif.

Friday Afternoon, May 13, 1960

2:00 P.M. Scientific Session: REGULAR PROGRAM
Napoleon Room

37. **Clinical Experiences With Fifteen Patients With Traumatic Rupture of the Thoracic Aorta.** Frank C. Spencer, Paul F. Guerin (by invitation), Hu A. Blake (by invitation), Washington, D. C., and Henry T. Bahnson, Baltimore, Md.
38. **Surgical Management of Penetrating Injuries of the Ascending Aorta and Aortic Arch.** Walter L. Diveley, Rollin A. Daniel, Jr., and H. William Scott, Jr., Nashville, Tenn.
39. **Antibiotics and Extracorporeal Surgery.** C. Frederick Kittle, and William A. Reed (by invitation), Kansas City, Kans.
40. **Achalasia of the Esophagus in Children.** Orvar Swenson, and Chris T. Oeconomopoulos (by invitation), Boston, Mass.
41. **Objective Evaluation of Surgery for Hiatus Hernia and Esophagitis.** Lucius D. Hill, and Kyle W. Chapman (by invitation), Seattle, Wash.
42. **Instrumental Perforation of the Esophagus.** Thomas F. Nealon, Jr., John Y. Templeton III, Vincent D. Cuddy (by invitation), and John H. Gibbon, Jr., Philadelphia, Pa.

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Original Communications

RADICAL LOBECTOMY

William G. Caban, M.D., New York, N. Y.*

This report defines a radical lobectomy as an operation in which one or two lobes of an entire lung are excised in a block dissection with certain of their regional hilar and mediastinal lymphatics.

The technical steps and clinical implications of the procedure to be discussed are based upon an experience with 48 radical lobectomies performed on the Thoracic Surgical Service of Memorial Center.

TECHNIQUE

In the description of the technique to follow, emphasis is placed upon the method of lymph node dissection The ligation and division of the tributary vessels and the bronchi to the various lobes are not included.

The first step of each radical lobectomy ideally proceeds from the most distal area of potential spread and works back toward the hilum and the tumor. However, this cannot always be achieved because adhesions and many other conditions in the thorax can obliterate clear anatomic planes. Instead of starting with the lymphatic dissection it may be necessary to begin at the hilum of the lobes by entering their fissures and proceeding distally, or by using a combination of these techniques. Another technical variant may be indicated when the tumor invades chest wall. It may be difficult to approach the hilum until this extension or peripheral fixation is mobilized to rest free, attached to the lung.

From the Thoracic Surgical Service, Memorial Center for Cancer and Allied Diseases, New York.

Made possible by the Albert Schweitzer Fund and contributions to the memory of Mr. Richard E. Myers

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To approach either lung, the patient is placed in a true lateral position. This is preferred to the supine or prone position, for it provides an optimum exposure for mediastinal lymph node dissection. The chest is entered through a long parascapular incision and the bed of the fifth or sixth rib. The pathologic setting is assessed, and if a radical lobectomy seems indicated and feasible and the patient's general condition is satisfactory, the procedure is carried out.

A Right Upper Lobe Radical Lobectomy (Fig. 1).—This procedure begins with the incision of the superior mediastinal pleura, from the apex of the chest to the azygos vein arch just anterior to the vagus nerve. Superiorly, a short horizontal limb is used to facilitate exposure of the subclavian artery and right recurrent laryngeal nerve.

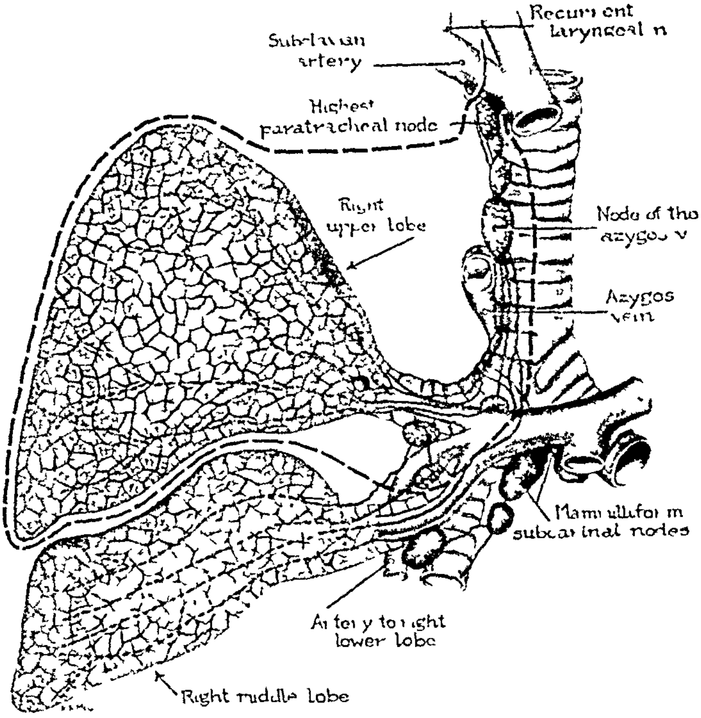

Fig 1—Right upper lobe radical lobectomy, anterior view Limit of excision diagrammed by interrupted line Note inclusion of nodes along the intermediate bronchus and the important azygos vein node Stump of right lower lobe bronchus shown, lobe omitted for clarity.

For the paratracheal dissection, the anterior pleural flap is elevated to the anterolateral surface of the superior vena cava, the phrenic nerve being displaced with it.* The posterior flap is mobilized as far as the vertebral bodies, leaving the vagus nerve uncovered. These flaps are retracted by the weight of the hemostats fastened to sutures attached to their free edges.

The azygos vein is transected between ties and ligatures, and the anterior limb lifted forward, thereby elevating the superior vena cava to some extent.

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*Although there are lymph nodes lying in the periphrenic areas as well as anterior to the superior vena cava and innominate veins, these nodes have not been included, for they lie beyond the arbitrary limits of the dissection as suggested by the superior vena cava. It was also thought that the route of lymphatic spread on the right side was predominantly paratracheal and retrocaval to the jugulo-subclavian junction.

The areolar tissue is cleared laterally and posteriorly from the superior vena cava from the apex of the chest to an area just beneath the azygos vein junction with it The upper thoracic portion of the vagus nerve is mobilized and the take off of the right recurrent laryngeal branch is identified The vagus is transected just distal to that point This facilitates a clearer dissection of the paratracheal areolar tissue

The apex of the dissection is the inferior border of the subclavian artery where a tongue of areolar, node bearing tissue is isolated and divided

Next, attention is directed to the trachea The fine connective tissue on its right lateral and anterior surfaces is found to separate readily, allowing the whole packet of tissue anterior to the trachea, including the areolar tissue posterior to the trachea and on the esophagus, to be swept downward off the innominate artery and aortic arch to the level of the pulmonary artery This can usually be done with division of only a few small vessels This packet of tissue represents the right paratracheal lymph node chain To maintain the integrity of this block of lymphatics, the dissection must be carried immediately adjacent to the large vessels and the trachea* Included in this dissection is the particularly important, constant, large node of the azygos arch lying just above the pulmonary artery It is the one most frequently involved in cancers of the right upper lobe This node is mobilized as the dense connective tissue superior to the pulmonary artery and behind the superior vena cava is incised This paratracheal node packet remains attached to the lung by peribronchial lymphatics and areolar tissue As each packet of nodes is mobilized, it should be tacked to a convenient point on the visceral pleura to keep them from obscuring the later dissection

An incision is then made in the interlobar fissure separating the upper lobe from the middle and lower lobes and carried down to the origin of the right upper lobe bronchus A group of nodes can be found surrounding the main stem bronchus The posterior nodes of this group are found near the anterior edge of the esophagus on the right On the left, they are less frequently found These are dissected toward the specimen

Lymph nodes are placed along the broncho arterial trees of each lobe, and it is important to note that the principal lymph node draining one lobe group may rest against the bronchus of an adjacent lobe The continuation of the right main stem bronchus to form the middle and lower lobe bronchi (intermediate bronchus) can be traced and it is usually feasible, and indeed of decided importance, to include the nodes that present themselves adjacent to these structures These are nodes that Borrie described as being in the "sump" position,[2] and usually represent the lowermost site of spread from right upper lobe lesions The division of the upper lobe bronchus can be helpful in providing a more thorough dissection of the retrocaval and peribronchial nodes

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*In order to accelerate the dissection of the small vessels in the mediastinum silver brain clips (McKenzie) are used for hemostasis instead of ligatures

It is necessary, on occasion, in the treatment of lesions of the right upper lobe, to include the middle lobe as part of the block dissection. Such a bi-lobectomy is usually performed for the following three reasons: (1) when there is a partial to almost total symphysis of these two lobes, (2) when the tumor transgresses one lobe and is fixed to or invades the other, and (3) when it is thought that a more complete dissection of the "sump" area along the intermediate bronchus can be obtained.

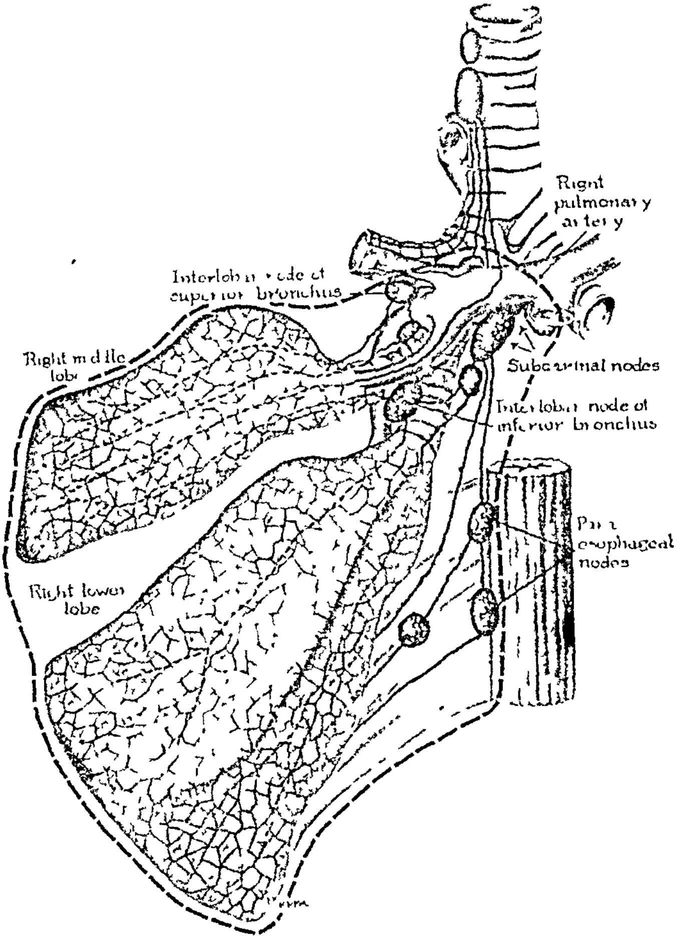

Fig 2.—Right middle and lower lobe radical lobectomy (anterior view) showing line of excision. Note inclusion of pre-esophageal, subcarinal, and interbronchial nodes Paratracheal chain may be removed as a separate specimen.

A Middle Lobe Radical Lobectomy.—It is improbable that the middle lobe would be removed by itself if cancer were suspected, except in the most unusual circumstances such as in very poor-risk patients. Tumors within it are almost always excised in combination with a right upper lobe radical lobectomy. To such a bi-lobectomy are added not only all the nodes in the "sump" area but as many as are available about the origin of the adjacent lower lobe bronchus as well.

At all times the indications for one operation or another are subject to flexibility and depend to a large extent upon the intrathoracic setting. For example, should the tumor extend between the middle and lower lobes, a lower lobe radical lobectomy en bloc with the middle lobe may be performed, leaving the right upper lobe intact. However, the lymph node dissection of the upper mediastinal and paratracheal nodes, including the azygos node, may then be done separately

A Right Lower Lobe Radical Lobectomy.—This dissection usually includes the middle lobe. It begins at the diaphragm, with a division between ligatures of the inferior pulmonary ligament[14] (Figs. 2 and 3). The esophagus is identified and the areolar and lymphatic tissue along its anterolateral surface is elevated upward as far as the inferior pulmonary vein and tacked to the lower lobe. Steady, gentle traction on the lower lobe in an anterior direction will expose the subcarinal node packet. At this level, this will become more available if the esophagus is retracted sharply posteriorly. The inferior and medial edge of the subcarinal packet is usually easily dissected from the adjacent pericardium. It is

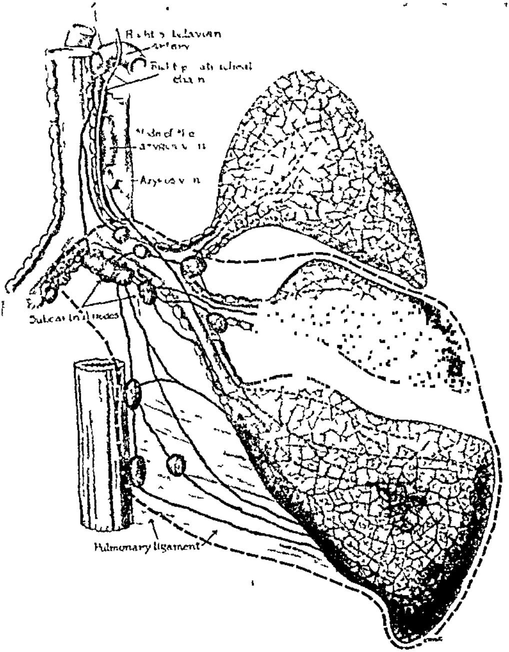

Fig 3 —Right middle and lower lobe radical lobectomy (posterior view)

not believed necessary, as some authors advocate,[3] to excise routinely a portion of the pericardium with this packet, for only the most filamentous areolar connective tissue lies between this lymph node group and the pericardium. By entering the plane adjacent to the posterior edges of the *left* or contralateral bronchial cartilages, simple and practically avascular mobilization of this nodal packet is effected.

Dissection is then carried to the main-stem bronchus, exposing its posterior surface. The origin of the right upper lobe bronchus is identified and the nodes are taken from the intermediate bronchus and reflected toward the specimen. After identifying the right middle and lower lobe bronchi, their transection at this time will permit the inclusion of the more cryptically placed nodes about the origin of the right middle lobe bronchus. The division of the tributary arteries and veins to these two lobes can then be made.

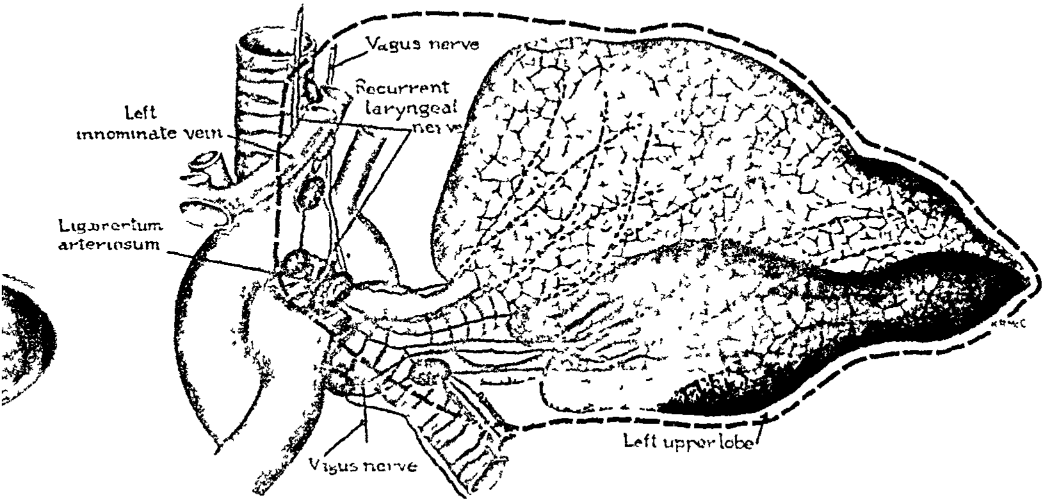

Fig 4 —Left upper radical lobectomy Interrupted line marks limits of dissection Note inclusion of interbronchial lymph node ("sump" position) between upper and lower lobe bronchi Subcarinal nodes removed as a separate packet

A Left Upper Lobe Radical Lobectomy (Fig. 4).—Incision is made into the mediastinal pleura, beginning at the apex of the chest and proceeding along the vagus nerve to the arch of the aorta. Its posterior limb follows the aortic arch to the level of the bronchus. Its anterior limb extends 1 to 2 cm. anterior to, and inferiorly along, the course of the phrenic nerve to the inferior pulmonary ligament to join the posterior incision.

Flaps are elevated and retracted. The phrenic nerve is fully liberated throughout most of its upper mediastinal course so that it may be retracted anteriorly and posteriorly by a Penrose drain as the dissection warrants.

The apex of the anterior mediastinal dissection is at the under surface of the left innominate vein at a point where it crosses the left subclavian artery. The areolar, node-bearing tissue is dissected off the vein, and several small branches must be separately identified and divided. The dissection proceeds anteriorly beneath the innominate vein as far as its entrance into the superior vena cava, dividing the highest intercostal and the thymic branches along the way This is the anterior limit of the dissection

The posterior limit of the dissection is the subclavian artery The packet of tissue is swept down off the subclavian, common carotid, and innominate arteries and the aortic arch The vagus nerve is carefully cleaned and, in particular, the large lymph node present in the space between the common carotid and subclavian arteries is included in the specimen

Beneath the aortic arch, the node of the ligamentum arteriosum* and that of the loop of the left recurrent nerve are freed Lying between the superior border of the pulmonary artery and the anterior surface of the left main bronchus and extending beneath the aorta is a packet of nodes which must be dissected down toward the specimen All of these are included with the previously dissected mediastinal packet of tissue and tacked onto the lung surface

The fissure between the upper and lower lobes is then divided and an approach made to the hilum The incision made into the visceral pleura is curved anteriorly and posteriorly to meet the incision made previously in the mediastinal pleura Starting with the bronchus to the left lower lobe, the important lymph nodes that are readily available in the "sump" position are swept upward between the lower lobe bronchus and its corresponding artery up to the take off of the upper lobe bronchus This last structure is isolated while dissecting the lymphatics toward the lung substance By division of the artery to the left upper lobe, the dissection of nodes from the superior border of the left main stem bronchus is facilitated and all these are included with those from the subaortic and anterior mediastinal dissections The subcarinal nodes are occasionally included as a separate packet This practice becomes more routine in light of the presence of metastases within them on several occasions

A Left Lower Lobe Radical Lobectomy (Figs 5 and 6) —This procedure is similar to that on the right, including the pre esophageal, subcarinal, and the peribronchial nodes ("sump" position) located along the left main stem bronchus and immediately available around the left upper lobe bronchus As on the right side, the left phrenic nerve is optionally crushed if a lower lobe is removed The lingular portion of the left upper lobe is not included although, as has been noted, the right middle lobe is taken as part of a right lower lobe radical lobectomy

Many patients who have a radical lobectomy performed are actual or potential pulmonary cripples, so that every effort is made to prevent compensatory emphysema of the lower lobes when an upper lobe lobectomy is performed The space previously occupied by the upper lobes has been filled as follows the parietal pleura occupying the dome and walls of the thorax is mobilized by extrapleural dissection so that it collapses on the superior surface of the lower lobe An Ivalon sponge is then inserted in this extrapleural space, after it has been autoclaved in saline, tailored to size and shape, and rinsed in 200 to 300 c.c. of a saline solution containing one million units of penicillin and one gram of streptomycin. Under-water drainage tubes are inserted separately, both into the pleural cavity and into this extrapleural space. The drainage of the pleural cavity is ended about the third or fourth day, and the extrapleural space about a day or two later. The extrapleural insertion of these Ivalon sponges has been performed in 8 instances without any morbidity or mortality. The longest period that one has been in place is 7 years (Fig. 7).

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*The ligamentum arteriosum has been divided in some instances to permit a more thorough node dissection beneath the arch of the aorta.

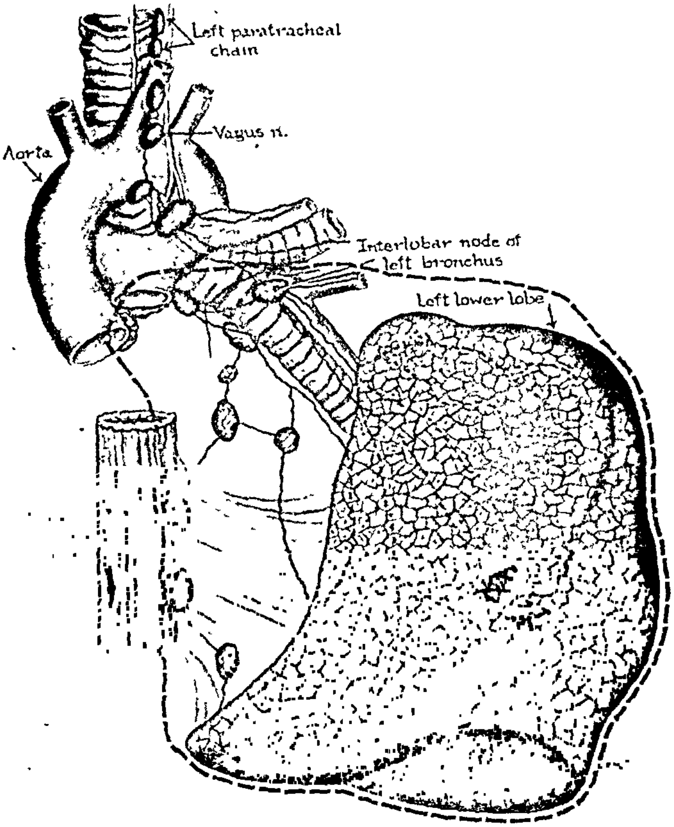

Fig. 5.—Left lower lobe radical lobectomy (anterior view). Interrupted line indicates limits of dissection. Note inclusion of the interbronchial node ("sump" position) as well as the subcarinal paraesophageal groups.

With the same principle in mind, there is the option of crushing the phrenic nerve after the excision of the middle and lower lobes. This causes an elevation of the leaf of the diaphragm which will fill to a large extent the space left by the lobectomies. The virtue of this, in preventing excessive compensatory emphysema of the right upper lobe as well as reducing dead space, must be balanced against the paradoxical respirations and attendant mediastinal swing that will occur.

INDICATIONS

In the following discussion it must be assumed that the pulmonary lesion is apparently contained within the confines of a lobe so that the transection of the lobar bronchus and vessels will provide a reasonable margin of uninvolved tissue. Such a determination can, in part, be made preoperatively by bronchoscopic visualization of the major bronchi. At the time of thoracotomy, palpation and limited dissection about the hilum will also help to decide the feasibility of a lobectomy. At best this is only a gross estimate of tumor boundaries and and can often be clouded by adjacent inflammation, fibrosis, and healed calcified tuberculous lymph nodes

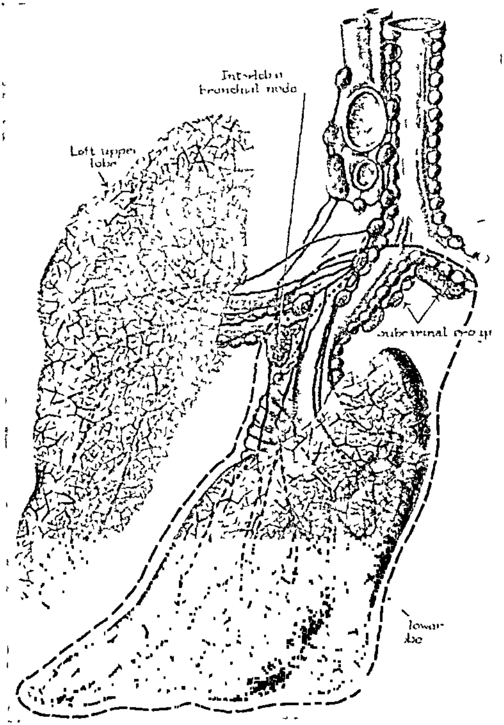

Fig 6—Left lower lobe radical lobectomy (posterior view).

There are two major indications for a radical lobectomy. These are for the treatment of (1) a primary cancer of the lung under certain circumstances, and (2) a lung tumor the nature of which is ambiguous.

Primary Cancer of the Lung.—The most important indication is for the excision of a peripherally placed cancer of the lung in a patient who, it is deemed, cannot withstand a radical pneumonectomy. The interpretation of what is ordinarily called "a poor-risk patient" varies from institution to institution and surgeon to surgeon. It is necessarily a flexible term because it is an appraisal of risk based upon not only fairly general measurements, but also subject to re-interpretation in the operating room. In other words, the patient who may be considered a good operative risk from the point of view of cardiorespiratory physiology may on occasion demonstrate bizarre physiologic responses to endotracheal intubation and the opening of his chest which would tend to modify the extent of the contemplated procedure. At this institution, reliance is placed upon a few arbitrary preoperative findings which might, either by themselves or in association with other abnormalities, influence the magnitude of the operation. For the most part, patients have been 75 years and over. They may have evidence of marked emphysema both by physical examination and maximum breathing capacity estimates, or they may have extensive myocardial disease. One condition that carries great weight in influencing decision in this regard is the history and finding of bronchial asthma.

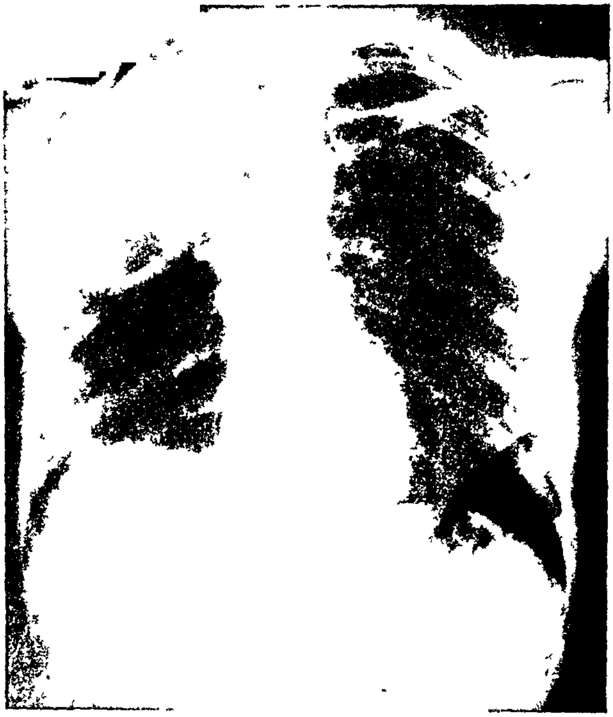

Fig. 7.—Postoperative roentgenogram of patient in Fig. 8 showing Ivalon sponge in right upper retropleural space and McKenzie clips in place along the paratracheal area. Note how little tracheal shift or diaphragmatic rise has occurred after a right upper and middle lobe radical lobectomy.

We do not at present elect to do a radical lobectomy for cancer of the lung as the treatment of choice. However, there is suggestive evidence that a right upper lobe radical lobectomy might become the preferred procedure for cancers grossly confined to the right upper lobe. Even now, some surgeons[9, 11] choose a simple lobectomy for these peripherally placed cancers, regardless of the clinical condition of the patient. Their experience will provide a base line of comparison for the value of adding the more extensive lymph node dissection.

Theoretically, a radical lobectomy might be less advantageous for primary lung cancers in the right middle and right lower lobes, for the usual lymphatic currents would tend to favor metastases at locations beyond the usual limits of a block dissection of a right middle and lower lobe radical lobectomy (although these may be excised as a separate specimen) The same is true for cancers in the left lower lobe Here the possibility of metastases extending first to the subcarinal and then contralaterally to the unavailable right paratracheal lymph nodes makes a more complete block extirpation difficult Lesions in the left upper lobe (particularly the superior portion) might have a more favorable outlook than those in the left lower lobe because their lymph node metastases tend to remain ipsilateral However, they too have a tendency to extend to the lymph nodes in the right by way of the subcarinal and anterior mediastinal channels

A Lung Tumor Whose Nature is Ambiguous—There are 2 clinical settings in which ambiguity surrounds the nature of a lung tumor (a) A cancer primary at another site is associated with a solitary lung shadow This lung shadow may represent either a separate primary lung cancer or a solitary metastasis[6] (b) A mass in the lung resembles cancer, but the diagnosis cannot be established with absolute finality, either before or during the operation

a In our experience, we have been impressed by the frequency with which multiple cancers, one of which is primary in the lung, have coexisted At Memorial Center we have collected 165 such cases In the same period of time (1926 to 1958), there have been 46 solitary metastases removed It is not safe, therefore, to presume that a solitary lung shadow, either synchronous or metachronous with a cancer elsewhere in the body, is a metastasis In fact, these figures suggest that it might be 4 to 1 in favor of its being a separate primary cancer* In either event, whether separate primary or metastasis, we know that local lymphatic extension can occur This does not need documentation in the case of primary cancer of the lung, but in 9 metastases to the lung removed by radical lobectomy, there were 6 instances in which daughter metastases existed in the hilar and mediastinal lymphatics (Table I) In other words, a metastasis from another site deposited within the lung parenchyma can behave as if it had its origin there and its metasteses can in turn proceed by lymphatic or venous routes

b As is so often the case, an area of inflammation will frequently be present in association with cancer of the lung This condition usually follows an obstruction of one of the bronchioles, which can produce distal atelectasis, pneumonia, and abscesses It is not always possible, by preoperative cytologic studies or by biopsy at the time of thoracotomy, to obtain a diagnosis either of a benign or a malignant process In other words, it is not infrequent at

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*In my article The Ambiguity of a Solitary Lung Shadow in the Presence of a Primary Cancer Elsewhere in Medical Science October 1958 a rule of thumb was given as an aid for the diagnostic dilemma If the patient has a squamous carcinoma elsewhere in the body the lung lesion is usually a separate primary and predominantly a squamous carcinoma as well If the patient has a soft part or skeletal sarcoma or melanoma elsewhere the solitary lung lesion is almost always a metastasis from these If there is an adenocarcinoma elsewhere there is about a 50 per cent chance of the solitary shadow being a primary lung cancer This probability may be higher if there is a lymphoma present

TABLE I. METASTASES TO LUNG

Number of cases		9
Positive extrapulmonic nodes		
Adenocarcinoma, breast	2	
Adenocarcinoma, rectum	1	
Teratocarcinoma, ovary	1	
Osteogenic sarcoma, femur	1	
Clear cell carcinoma, kidney	1	
	6	
Negative extrapulmonic nodes		
Fibrosarcoma, thigh	1	
Melanoma, skin of axilla	1	
Rhabdomyosarcoma, thigh	1	
	3	

the time of exploratory thoracotomy that repeated biopsies and frozen section analysis of suspicious lung areas can be reported as showing chronic inflammation. This leaves in doubt whether these sections are truly representative, or whether there is a more cryptically placed cancer.* In this equivocal setting it is probably wisest to assume cancer to be present.† As a compromise, therefore, a radical lobectomy is performed. This operation, while fulfilling the desirability of removing the tumefaction in the lung and many of its regional lymphatics, does not subject the patient to the increased hazard of a pneumonectomy.

RESULTS

There were 48 radical lobectomies performed in the 7-year period from March, 1951, to March, 1958. The first was performed in March, 1951. The patient, a woman, had had an adenocarcinoma of the rectum removed 9 years previously, and a solitary shadow appeared in the left upper lobe. She underwent a left upper lobe radical lobectomy and the pathologic report showed a "metastatic adenocarcinoma consistent with rectal origin." There were two positive mediastinal lymph nodes found in the supra-aortic packet (anterior mediastinal chain) that was part of the dissection. The patient is without evidence of disease 8 years and 4 months later (July, 1959).

In this series there were no postoperative complications other than those which caused 5 postoperative deaths: one from gastrointestinal hemorrhage, one caused by overwhelming infection, another by a myocardial infarct, a fourth by hemorrhage in the operating room with cardiac failure, and one from an undetermined cause. This last occurred in a woman who had had a right middle and upper lobe radical lobectomy performed in July, 1954, for an adenocarcinoma of the lung, and the last operation was a left upper radical lobe lobectomy in December, 1955, for terminal bronchiolar carcinoma which was probably a separate primary cancer

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*There may be some question as to the advisability of a biopsy by aspiration or incision of a suspected lung tumor. This applies also to the excision of individual lymph nodes from the mediastinum. Spjut[12] found malignant cells in pleural cavity washings of 13 of 28 patients who had lobectomy, pneumonectomy, or exploratory thoracotomy along with excision of tissue for frozen section. Only 3 positive washings were obtained from 21 patients who had resection not preceded by biopsy. Although such free-floating cells are of apparently frequent occurrence, it is unusual to find new actual implants that could be directly attributed to them. However, one wonders if the manipulation and traumatization attendant upon these biopsies does not promote hematogenous dissemination. In addition, if the suspected lesion is active tuberculosis, incisional biopsy can cause spillage of the tubercle bacilli into the pleura.

†Just recently, a lesion removed by wedge excision and appearing grossly and by frozen section as a tuberculoma was found on paraffin section to have terminal bronchiolar carcinoma at its periphery. This finding of cancer in juxtaposition with healed tuberculosis is not uncommon.

This mortality rate is high There is no reason, however, to attribute any of the deaths to the more elaborate lymphatic dissection, a contention that is supported by the fact that there have been no postoperative complications or mortality in the last 13 radical lobectomy patients Over one half of these operations were performed by the surgical residents under supervision as one of their earliest thoracic procedures

Primary Lung Cancer—There were thirty four primary lung cancers removed The histologic types most commonly found (Table II) were present, except oat cell carcinoma In this group, 11 had lymph nodes containing cancer beyond the limits of a simple lobectomy

Table II Primary Lung Cancer

Number of cases		34
Contents of lymph nodes not mentioned		2
Determinable cases		32
Positive extrapulmonic nodes		
Epidermoid	3	
Terminal bronchiolar	4	
Anaplastic	1	
Adenosquamous	1	
Adenocarcinoma	2	
	11/32 = 34%	
Negative extrapulmonic nodes		
Epidermoid	7	
Terminal bronchiolar	5	
Adenocarcinoma	4	
Muco epidermoid	3	
Anaplastic	1	
Pleomorphic reticulum cell sarcoma	1	
	21/32 = 66%	

Five or more years ago, 4 patients with primary lung cancer had a radical lobectomy (Table III) Two of these had negative hilar and mediastinal lymph nodes One died 27 days postoperatively of a myocardial infarct, and the other is alive and well having had a terminal bronchiolar carcinoma of the right lower lobe Two patients had positive extrapulmonic lymph nodes, one, who is alive and well 7 years later, had an adenosquamous carcinoma of the right upper lobe, one died of disease 13 months postoperatively

Three to 5 years ago, 18 patients were operated upon In this group there were 5 patients who had extrapulmonic lymph nodes containing metastases Of these 5, 2 died postoperatively, 2 died of disease 18 and 26 months postoperatively, and one was without evidence of disease and lost to follow-up 12 months postoperatively Eleven patients had negative hilar and mediastinal

TABLE III. 5-YEAR SURVIVALS OF PATIENTS AFTER RADICAL LOBECTOMY FOR CANCER

Patients operated on *5 or more years* ago		8
Primary lung cancer	4	
Metastases to lung	4	
Patients with *positive* mediastinal nodes		5
Alive and well, 5 or more years		3
Conditions of 5-year survivors with *positive* mediastinal nodes:		
1 primary adenosquamous carcinoma of lung		
1 metastatic rectal carcinoma		
1 metastatic teratocarcinoma of ovary		
1 osteogenic sarcoma (died of disease 7 years after radical lobectomy)		
Patients with *negative* mediastinal nodes		2
Died postoperatively		1
No evidence of disease		1

lymph nodes. Six of these are alive and well 3 to 5 years later. Three died of disease 17, 24, and 30 months postoperatively; one died 23 days postoperatively. In 2 patients the state of the mediastinal lymph nodes was not mentioned. One of these patients died of disease 6 months postoperatively, and the other was alive and well over 3 years later.

Metastases.—Of the forty-eight radical lobectomies, nine were performed for metastases to the lung. There was no postoperative morbidity or mortality in this group. The sites of origin are shown in Table I.

Of these 9 patients, 6 had hilar and mediastinal lymph nodes containing cancer beyond the limits of excision of a simple lobectomy.

Five or more years ago, 4 patients in this group had excision of metastases to the lung (Table III). Three of them had positive mediastinal lymph nodes. These included metastases from rectal cancer, a teratocarcinoma of the ovary (Fig. 8), and 1 osteogenic sarcoma. The first 2 are alive and well, and the third died of disease 7 years after radical lobectomy. The one patient who had negative mediastinal lymph nodes in the radical lobectomy specimen had a melanoma metastasis and will be described below.

In the period 3 to 5 years ago, 1 patient with a pulmonary metastasis had a radical lobectomy. This metastasis was from a renal carcinoma, and daughter metastases in the mediastinal lymph nodes were found. The patient died 6 months later of cerebral metastases.

Position of Tumor.—In the group of primary lung cancers, there were four in the right upper lobe, four in the right middle and lower lobe, and three in the left upper lobe.

In the group of metastases to the lung with postive extrapulmonic lymph nodes, there were three deposits in the right upper lobe, one in the left upper lobe, one in the right lower lobe, and one in the left lower lobe.

Multiple Primaries.—There were six double primary cancers, one of which was of the lung. Other sites included: 2 tongue, 2 breast, 1 larynx, and 1 lung.

Benign Conditions.—There were five radical lobectomies performed for tumor-like lung conditions that subsequently proved to be benign. These included 4 chronic pneumonias with atelectasis and/or abscess, and 1 lipoid pneumonia.

There were no complications or mortalities in this series.

COMMENT

In reviewing the results that have been listed in the previous section, it can be seen in Tables I and II that of 41 patients operated on either for primary or metastatic cancer to lung by means of a radical lobectomy, 17 (or about 42 per cent) had metastatic hilar and/or mediastinal lymph nodes when these were analyzed. In other words, 42 per cent had more cancer removed by a radical lobectomy than would have been removed had a simple lobectomy been performed.

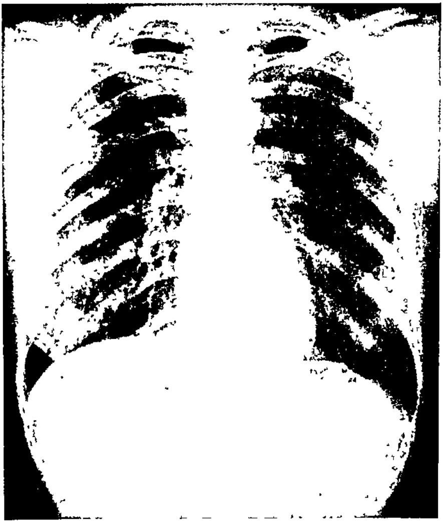

Fig 8.—Roentgenogram showing metastatic teratocarcinoma of ovary in right upper lobe. Patient had right upper and middle lobe radical lobectomy. The specimen contained a daughter metastasis in the azygos vein node. Patient is without evidence of disease 8 years later.

Of these 17 patients with positive extrapulmonic lymph nodes, 8 were operated on 5 or more years ago, and 3 are alive without evidence of disease at this time. In these individuals, at any rate, it is quite probable that they owe their prolonged survival to the inclusion of these extrapulmonic lymph nodes, although there may have been contributory factors which are hard to analyze and document, such as host resistance. This term, host resistance, is an all-embracing one and may prove to possess several components. It attempts

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Multiple Primaries.—There were six double primary cancers, one of which was of the lung. Other sites included: 2 tongue, 2 breast, 1 larynx, and 1 lung.

Just what extra chance for survival is afforded by the inclusion of the lymph nodes as part of a radical lobectomy or radical pneumonectomy is difficult to determine at present because of the limited number of procedures performed. The same is true in defining prognosis derived from the pathologic material alone.

Although a tentative attitude is necessary at this time, one fact seems to be evident: each case is a law unto itself, and survival probably is the result of the interplay of various pathologic states with the intangible forces of host resistance. It is therefore unwise to permit a single, isolated clinical or pathologic feature (for example, the threat of blood vessel invasion or the finding of a single mediastinal lymph node positive for cancer) so to dominate the picture that all aggression ceases. Instead, it would seem wiser to advocate an operation that attempts to eradicate most of the tangible elements in lung cancer, thus leaving less to chance. To our mind, a radical pneumonectomy and a radical lobectomy best fulfill this purpose.

SUMMARY

1. A radical lobectomy can be defined as an operation in which one or two lobes of an entire lung are excised in a block dissection with certain of their regional hilar and mediastinal lymphatics. This is to be distinguished from a simple lobectomy, which is an operation restricted to a lobe or lobes alone.

2. The pathologic rationale for including the hilar and mediastinal lymph nodes in either a radical lobectomy or a radical pneumonectomy is the finding based upon autopsy material that the lymph nodes are the most frequent sites of metastases from cancer of the lung. This fact is further confirmed by studies of lymph node specimens removed by these operations, at which time it was noted that metastases were present in them regardless of size, position, and histologic type of the primary tumor. In addition, autopsies on patients who had only a simple pneumonectomy or lobectomy for lung cancer revealed that there was recurrence in the ipsilateral mediastinal lymph nodes in 28 and 21 per cent, respectively.

3. The technique for removing each lobe with its regional lymphatics is described and diagrammed.

4. There are two major indications for a radical lobectomy. It is used to excise (a) a peripherally placed primary cancer of the lung for those who cannot tolerate a radical pneumonectomy, and (b) a lung tumor whose nature is ambiguous by reason of its association with a primary cancer at another site. It is also used for those tumefactions whose nature remains equivocal even at operation.

5. Results from 48 radical lobectomies, from 1951 to 1958, are listed. These were performed for 34 primary lung cancers, 9 metastases to the lung, and 5 benign, tumor-like conditions.

6. In those patients who had a radical lobectomy either for a primary cancer or a metastasis to the lung, 41.5 per cent had hilar and mediastinal lymph node metastases.

7. Eight patients were operated on 5 or more years ago, and 5 had positive mediastinal lymph nodes. Three of these are alive and well without evidence of disease.

8. The survival for 5 or more years of those who had excision of cancer-containing hilar and mediastinal lymph nodes is attributed in large part to the more extensive lymphatic dissection associated with a radical lobectomy.

9. It is believed that the careful study of excised hilar and mediastinal lymph nodes as part of a radical lobectomy or pneumonectomy provides a valuable basis for prognosis. The pathologic study of these lymph nodes, together with the knowledge of the histology of the primary cancer and evidence of blood vessel invasion by tumor are three essential aids in forecasting survival.

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PROGNOSTIC FACTORS AND RESULTS OF TREATMENT IN PYOGENIC PULMONARY ABSCESS

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THERE is little doubt that the advent of antibiotics has significantly affected the incidence and results of therapy of pulmonary abscess as well as other types of pulmonary infection. Acute bacterial pneumonitis is less common and its course is often aborted so that the secondary complications of empyema and abscess develop less frequently. However, certain patients fail to respond well to antibiotics and suffer a fatal outcome; others achieve resolution of the acute inflammatory process but are left with residual lesions necessitating operation to accomplish complete cure.

In order to examine more carefully this changing picture and to isolate, if possible, prognostic factors which would be useful in predicting the course of therapy, all patients with pulmonary abscess admitted to this hospital during the 10 year period prior to Jan. 1, 1959, were reviewed.

MATERIAL

During this period 90 cases of primary pyogenic pulmonary abscess were treated. Abscesses secondary to other conditions, such as carcinoma, pulmonary cysts, or tuberculosis, were excluded.

Most patients were from a low economic stratum or were indigents, and the proportion of elderly patients was high (Table I). Sixty per cent of the patients were over 50 years of age and over 35 per cent were over 60 years of age. There was a high incidence of significant associated disease which was of considerable import, both in leading to the development of abscess and in aggravating the course of the disease, frequently contributing to a fatal outcome.

Only a few patients were young and in good general health, factors which are reflected in the accumulated results.

The anatomic distribution of these lesions did not vary significantly from that in other reports, and the usual predominance in the right lung and in the upper portions of each lung was again noted. This distribution is most readily explained on the basis of aspiration although in only 9 cases (10 per cent) was there a history which clearly suggested aspiration.

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TABLE I. AGE DISTRIBUTION

YEARS	NUMBER
0- 9	2
10-19	0
20-29	6
30-39	10
40-49	18
50-59	22
60-69	19
70-79	11
80-89	2
Total	90

ETIOLOGY

Poor oral hygiene has been frequently incriminated as an etiologic factor. In this group of patients, 63 had definitely carious teeth, 16 patients had teeth in good repair, and 11 were edentulous.

Twenty cases followed an episode of acute bacterial pneumonitis, 5 being pneumococcal in origin.

In 9 cases there was a probable source of aspiration. Four patients had had preceding dental extractions, 2 had had tonsillectomies, 2 had had acute alcoholic bouts with stupor and emesis, and 1 patient had had a severe purulent sinusitis.

Four patients had had a preceding cerebrovascular accident with coma and 4 had chronic epilepsy, conditions which may well have predisposed to aspiration, although a definite history could not be elicited.

THERAPY

All patients had essentially similar initial medical therapy. In general, this consisted of appropriate antibiotics, postural drainage, and supportive measures. Bronchoscopy was performed in most cases, both diagnostically and therapeutically. Removal of bronchial plugs and associated forceful coughing following bronchoscopy frequently resulted in prompt evacuation of filled cavities, contributing to more rapid resolution of the acute inflammatory reaction.

X-ray studies were made at intervals and, as long as resolution of the inflammatory process progressed and the size of the cavity diminished, the medical program was maintained. Operation was considered whenever progress seemed to have become arrested or if there was residual cavitation after resolution of the acute inflammatory process. In 8 cases, the abscess was drained early in the patient's course, usually because of cavities which did not empty well or because of overwhelming toxic reaction.

RESULTS

Since all patients received similar initial therapy, the results of medical treatment can be divided conveniently into three categories based on the response to medical treatment. In the first group are the patients who achieved a satisfactory result with medical therapy alone, with subsidence of inflammatory reaction and closure of cavities. In the second group are those patients who died while receiving medical therapy. In the third group are those in whom surgery was required to accomplish cure. The last group, of course, represents a large measure of medical success, since patients coming to resection have ordinarily obtained a subsidence of inflammatory reaction and operation is performed for control of residual lesions, particularly open cavities.

According to this classification (Table II), only 32 patients of 90 achieved a satisfactory result on medical therapy alone.

TABLE II. RESULTS

Patients treated medically:			
1. Satisfactory		32	(35%)
2. Fatal		21	(23%)
a Due to abscess	11		
b Due to associated disease	10		
Patients requiring operation		38	(42%)

Twenty-one patients died while undergoing medical therapy. Analysis of the causes of death in these cases revealed two important factors: the patient's age and concomitant disease. Table III illustrates the comparative age of patients who died and those who survived. There was a striking increase in mortality rate in elderly patients and in children; only 4 of 13 patients over 70 years of age and neither of the children (aged 2 and 4 years) survived.

TABLE III. RELATION OF AGE TO RESULT

AGE IN YEARS	MEDICALLY TREATED		SURGICALLY TREATED
	SATISFACTORY	FATAL	
0 9	0	2	0
10 19	0	0	1
20 29	3	1	1
30 39	5	1	4
40 49	5	0	11
50 59	11	2	11
60 69	6	6	7
70 79	2	7	2
80 +	0	2	0

In 11 of these 21 patients (12 per cent of the total number of 90), death was thought to be due primarily to the pulmonary abscess. Three patients died of direct complications, one death resulting from massive hemorrhage and two from acute perforation with bronchopleural fistula and empyema. Eight patients died as a result of uncontrolled infection; the ages of these patients were 76, 72, 80, 77, 88, 38, 63, and 57 years, emphasizing the effect of age.

In 10 patients death was thought due primarily to other causes: 4 patients died with cerebrovascular accidents, 2 patients had multiple systemic abscesses including cerebral abscesses which were thought to be the principal cause of death, 1 patient died in cardiac failure, 1 with enterocolitis, and 1 with massive gastrointestinal bleeding.

Thirty-eight patients required surgical treatment, 31 having resection of residual lesions and 7 having drainage of the abscess, usually in an attempt to control overwhelming infection. Four patients died of surgical complications following resection and 4 died of unremitting infection following drainage.

PROGNOSTIC FACTORS

Duration of Symptoms (Table IV).—The highest incidence of successful treatment with medical therapy alone was found in the group of patients who had symptoms less than 4 weeks prior to admission to the hospital. Over two thirds of the patients with symptoms present longer than 8 weeks prior to admission eventually required surgical treatment. No correlation could be established between the duration of symptoms and the likelihood of death.

TABLE IV. DURATION OF SYMPTOMS*

WEEKS	SURGICAL TREATMENT	MEDICAL TREATMENT
0- 4	7	26
4- 8	4	9
8-12	13	3
12 +	8	6

*Only patients giving an accurate history are tabulated.

Bacteriologic Studies.—The distribution of organisms identified in the sputum of each group is shown in Table V. The most commonly identified organisms were *Staphylococcus aureus* and *Streptococcus viridans*. There was a scattered distribution among a number of types, each of which occurred in relatively small numbers. The most striking finding was in the group of staphylococcal infections, only 20 per cent of the patients obtained a good result by medical therapy alone, the remainder either requiring operation or succumbing to infection.

TABLE V. BACTERIOLOGIC ETIOLOGY*

	MEDICALLY TREATED		SURGICALLY TREATED
	SATISFACTORY	FATAL	
Staphylococcus aureus	6	9	15
Streptococcus viridans	18	6	17
Escherichia coli	5	6	3
Hemophilus influenzae	3	2	3
Pneumococcus	2	4	0
Anaerobic streptococcus	1	0	2
Enterococcus	2	0	1
Pyocyaneus	0	0	1

*In many cases more than one organism was present on repeated culture.

Location of Abscesses.—The location of abscesses in relation to prognosis is given in Table VI. Lower lobe cavities appeared to be appreciably more resistant to medical therapy. Less than 20 per cent of this group obtained a satisfactory result with medical therapy alone; approximately one half of these patients eventually required operation and an additional 30 per cent died while on medical therapy.

TABLE VI. LOCATION OF ABSCESSES

	MEDICALLY TREATED		
	SATISFACTORY	FATAL	SURGICALLY TREATED
Upper lobe	22	10	21
Middle-lingula	3	1	0
Lower lobe	7	10	16

Size of Cavity.—The relative size of cavities in these groups of patients is illustrated in Table VII. In a few cases original roentgenograms were not available, or for other reasons the size could not be estimated with reasonable accuracy. The most striking feature in this analysis was found in the results of treatment of large cavities. In patients with cavities 6 cm. in diameter or greater, only 2 of 20 achieved a satisfactory result by medical therapy alone; 9 patients succumbed to infection and 14 eventually required operation. The prospect for a successful result with medical therapy was much better in patients with cavities less than 2 cm. in diameter; nevertheless, even in these smaller lesions, a number of patients eventually required surgical treatment for complete obliteration of cavities.

TABLE VII. SIZE OF CAVITY

	MEDICALLY TREATED		
CENTIMETERS	SATISFACTORY	FATAL	SURGICALLY TREATED
0 2	11	7	7
2 4	11	3	12
4 6	8	2	4
6 +	2	9	14

DISCUSSION

Despite the advent of antibiotic therapy and improvement of surgical techniques, pulmonary abscess continues to be a formidable disease. A rather wide variation in mortality rate has been noted in reported series,[1-4] in general tending to reflect the influence of the type of patient treated rather than the method of treatment.

It has been noted in this study that certain incidental factors are of serious import, particularly the age of the patient and associated or coincidental diseases. The percentage of good results of medical therapy in this series is lower than that reported by others,[1-5] probably reflecting the status of the patient and the abscess rather than a true variance in results, since the usual medical regimen is rather well standardized. It has become highly unusual for the patient who is reasonably young and in good general health to succumb to overwhelming infection associated with pulmonary abscess. In the present series, only 1 patient between the age of 10 and 50 died of pulmonary infection and 1 other patient in this age group died with a sudden massive hemorrhage. In approximately 50 per cent of the patients who died, death was thought due to other disease rather than to the abscess, which was being adequately controlled. Most of the patients whose death was thought primarily due to the abscess were elderly and debilitated patients. However, the 11 patients in whom death was thought due to the abscess represent potentially curable cases. It is conceivable that early drainage of the abscess might have improved the results in this group.

Although Fox, Hughes, and Sutliff[2] have also noted an increased percentage of patients requiring operation with increased duration of symptoms prior to admission, relatively little attention has been given to other specific factors which are important in their influence on the course of the disease. In predicting the eventual outcome of the disease and anticipating which patients will be likely to require operation, the present analysis may be useful. If it can be predicted with a high degree of probability early in the course of the disease that operation will eventually be required, it is possible to prepare the patient physically and psychologically from the time of admission. Although none of the factors studied is an absolute prognostic guide, when taken in combination they provide a good index of the probable outcome and can lead to a more efficient therapeutic regimen.

SUMMARY

1. Ninety consecutive cases of primary pyogenic pulmonary abscess have been studied.

2. Thirty-two of 90 patients achieved a good result with medical therapy lone, 21 died while on medical therapy, and 38 patients required operation.

3. Of the 21 fatalities among patients on medical therapy, death was hought due primarily to the abscess in 11 cases which represent potentially urable patients with more effective treatment of the abscess. The other 10 patients succumbed to associated diseases.

4. Certain factors strongly indicated the likelihood of failure of cure by medical therapy alone. In descending order of certainty, these factors were as follows: (a) size of cavity 6 centimeters or more in diameter, (b) a history indicating onset of disease earlier than 8 weeks prior to admission, (c) staphylococcal infection, and (d) location of abscess in lower lobe of either lung.

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THE ANTERIORLY CRUSHED CHEST OR "STEERING-WHEEL INJURY"

An Improved Method for Sternal Traction

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Crush injuries of the chest are classified into (1) anterior, (2) lateral, and (3) posterior varieties,[1] and, of these, the anterior is particularly pernicious. Although it may occur in a variety of ways, the anteriorly crushed chest derives its pseudonym, "steering-wheel injury," from the fact that it occurs most commonly in automobile accidents when the driver of the vehicle is hurled forward by momentum over the steering post. It is the purpose of this report to present an improved method for applying sternal traction in this type of injury, to present a case in which the method was used, and to discuss briefly associated problems.

At the time of impact, sudden posterior displacement of the sternum produces fractures superiorly across the sternum, laterally across the ribs or costal cartilages on both sides, and occasionally inferiorly across the sternum as well, resulting in an unstable or "floating" section of anterior chest wall. Unless corrected, increasing respiratory insufficiency occurs, due to several associated mechanisms.

1. The "floating" segment of anterior chest wall moves paradoxically inward with inspiration and outward to neutral position with expiration, which produces a condition resembling a large sucking wound of the chest. Added respiratory effort is required in compensation.
2. Further reduction in ventilatory ability results from the attempt to minimize pain by minimizing excursions of the chest, with resultant inefficient rapid and shallow breathing.
3. Cough becomes inefficient because of the mechanical disruption of the thoracic cage, because of pain, and because of drugs given to alleviate the pain.
4. When cough is inefficient, secretions normally present are not efficiently expelled; but to make matters worse, reflex motor and secretory stimulation of the bronchial tree follows trauma to the chest, with resulting bronchorrhea, bronchospasm, and edema of the bronchial mucosa.[2, 3] Excessive production of pulmonary secretions coupled with marked interference with their evacuation results in "wet lung," followed by atelectasis and pneumonitis and progressive diminution in respiratory capacity and reserve.

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5. Ileus is an almost constant concomitant of severe chest injury. The gastric and intestinal dilatation produces elevation and restriction of the diaphragm and further loss of ventilatory capacity.

6. Mediastinal compression, immediate and acute, may be a significant cause of rapid deterioration. In addition, the inflow of blood to the heart through the great thin-walled veins of the chest, which is significantly assisted by the pumping and sucking action of fluctuations in the normally subatmospheric intrathoracic pressure, may be decreased to an alarming extent as negative pressure is reduced or, at times during the respiratory cycle, even abolished.[1]

The clinical picture is that of restlessness and anxiety, shock, cyanosis, tachycardia, rapid shallow breathing, and painful and ineffective cough. The lungs become filled with secretions. Movements of the floating segment may be slight at first, but, with gradually increasing embarrassment to respiration, marked increase in the amplitude of the paradoxical movement develops.

To reverse this disastrous sequence of events, stabilization of the floating segment must be accomplished. With stabilization, pain is minimized, ventilation improves, cough becomes effective, secretions are expelled, and the vicious cycle is interrupted and reversed. Methods of stabilization may be divided into (1) methods of internal fixation, (2) methods of external fixation by traction, and (3) Mörch and Avery's method of internal pneumatic stabilization by respirator.[18]

Internal fixation has been attempted by transfixion of the fractured ends of the sternum or ribs with Kirschner wires,[4] or by attempting to hold the fractured ends with wire or silk sutures.[5] Intramedullary nailing of the fractured ribs has also been attempted.[6] Methods of internal fixation have not been particularly satisfactory in cases of rib fractures, and even less so for the anteriorly crushed chest.[7] In such cases, internal stabilization is usually incomplete, inadequate, and insecure, and often lost as rib ends fragment or pins migrate.

Where feasible, traction is the most satisfactory way of restoring the integrity of the chest wall. As a mechanical result of the direction of the fracturing force and the direction of the resulting multiple fractures, the "floating" segment in anteriorly crushed chest is unstable inwardly; and traction applied in the opposite direction to that of the fracturing force will lock the fragments back in normal anatomic and functional position and produce a stable chest wall. The situation may be illustrated simply by comparing the crushed chest to a collapsible drinking cup, which loses its stability when collapsed, but becomes firmly rigid when the ends are distracted (Fig. 1). In addition to immediate correction of the fundamental disturbance, allowing more efficient ventilation, easier cough, and evacuation of secretions, the application of secure traction immediately expands the chest and increases the capacity of the lung for respiration and ventilation. Furthermore, traction allows healing in a more expanded chest position and makes for a better functional end result.

Various methods for the application of traction in anteriorly crushed chest injuries have been suggested. Towel clips and cervical tenacula have been used to grasp the ribs or costochondral fragments adjacent to the sternum, and wires have been passed about the fragments.[8, 9, 10] Cervical tenacula have been applied across the sternum, with points in the opposite interspaces.[11, 12] Towel clips or cervical tenacula have been used to apply traction through drill holes in the anterior sternal table, with the points of the instruments approximated in the sternal marrow cavity. Specially designed tongs[13, 14] have been applied through drill holes in the anterior table of the sternum in similar manner. Wires have been threaded through holes in the anterior cortex. Various types of hooks have been screwed into the anterior cortex of the sternum to provide a purchase for traction, including coat-hanger hooks,[15] corkscrews and cup-hooks.[1] Hudson, McElvenny, and Head[7] have suggested an interesting method of soft-tissue traction using multiple subcutaneous Kirschner wires attached to spreader bows, adapted particularly to certain forms of the lateral types of crushed chest.

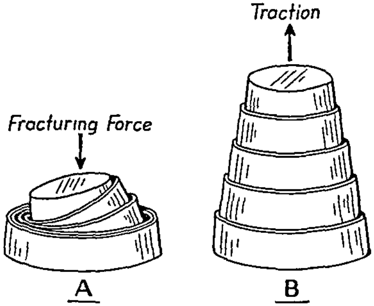

Fig 1.—The anteriorly crushed chest may be likened to the collapsed drinking cup, with traction the fragments lock and stability is achieved

It is apparent, from the very variety of suggested methods of sternal traction, that none is completely satisfactory and universally adaptable. One of the major faults with the numerous devices has been the lack of security. Fragmentation of bone and loss of anchorage often occurs with the application of prolonged and adequate traction force and this leads to the necessity for reducing and compromising with the weight applied. Leverage may be considerable and may cause fragmentation and loss of purchase in spite of meticulous and delicate care.

PROCEDURE

We have simply and effectively resolved these mechanical difficulties in applying and anchoring traction devices by passing a Kirschner wire *underneath* the sternum in the center of the floating segment, through the retrosternal space,[16] using the wire as a yoke through which traction is applied. This method provides strong, secure, and dependable anchorage through the full thickness of the sternum rather than through one fragile cortex, permitting application of as much force as desired without fear of distraction or loss of purchase as the days progress. There is no leverage to loosen the purchase, and the direction of pull can be changed as desired along the axis of the Kirschner wire, affording easy mobility to the patient in bed, who can sit up or lie down while traction is continuously exerted. The procedure is as follows:

> A generous incision is made transversely across the chest over the center of the floating segment and carried to the intercostal spaces on either side. The internal mammary vessels may be ligated, or may be avoided by staying close to the sternum. A grooved director is bent about 1.5 cm. from its tip to a 60-degree angle, and the shaft of the director itself is gently curved concavely, as illustrated in Fig. 2.

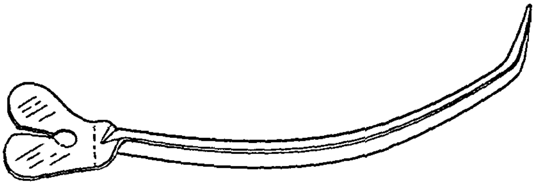

Fig. 2—A grooved director is bent as illustrated.

> The director is then passed under the sternum in the center of the floating segment, with care to avoid entering either pleural space. The tip of the director is maintained in apposition to the body of the sternum at all times. A flexible Kirschner wire is passed through the groove in the director, and the director is then removed, leaving the wire in place (Fig. 3). The ends of the wire are carefully secured with a Kirschner wire spreader bow, and traction immediately applied. The patient's condition improves at once. The incision is closed, and weights applied through a system of pulleys. The patient is allowed considerable mobility in bed. There is no danger of leverage loosening the purchase, nor of excessive weight tearing out the moorings. We have used 20 pounds of traction initially, and continued traction for about 3 weeks with gradual reduction in weight terminally. The procedure may be performed under local anesthesia, although we have preferred the complete control of respiration afforded by endotracheal intubation under topical anesthesia, followed by light general anesthesia, with suctioning of the tracheobronchial tree and administration of 100 per cent oxygen.

Patients in whom the chest wall is so comminuted that traction will not lock the fragments into position can now be successfully treated by "internal pneumatic stabilization," using the brilliantly conceived Mörch respirator attached to a tracheotomy.[16] This method represents a singularly striking advance in the therapy of severe, previously fatal, crushing injuries. While truly lifesaving in these cases, the method is associated with morbidity and complications, and requires constant careful and meticulous attention to detail over a prolonged period of time. In situations where adequate stabilization can be achieved by traction, this is much to be preferred, being simple and easier, and returning the patient more rapidly and completely to a self-sufficient physiologic state.

Next in importance to actual stabilization of the chest is tracheotomy, and this should be routinely employed. Its value has been amply demonstrated.[17]

Tracheotomy allows aspiration of secretions, diminishes dead space, and diminishes the effort of breathing by removing nasal and pharyngeal resistance Tracheotomy should complement, not replace, correction of the basic defect by skeletal traction, which remains of prime importance and the cornerstone of therapy Nasogastric or intestinal intubation to relieve gastric dilatation and abdominal distention secondary to the paralytic ileus is an important measure

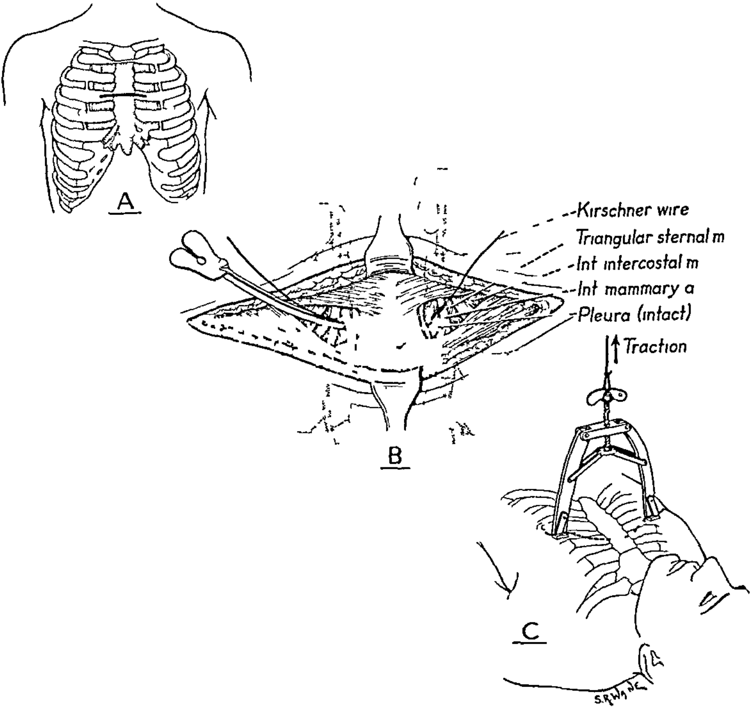

Fig 3 —*A*, The skin incision in relation to the fractured segment

B The grooved director has been passed from one side of the sternum to the other, and the Kirschner wire has been passed through the groove Following this the director is carefully removed leaving the wire in place

C, A Kirschner wire spreader is securely attached to the ends of the wire and continous traction immediately applied

Antibiotics are indicated to prevent and treat pneumonitis In addition, supportive therapy must be given as necessary, including blood, intravenous fluids, oxygen, and careful tracheotomy care Other serious injuries may be associated with the crushed chest, including pneumothorax, hemothorax, tracheal or bronchial rupture, cardiac laceration and tamponade, diaphragmatic rupture, and extrathoracic injuries and must be treated as indicated

CASE REPORT

The following illustrative case is presented:

Mr. W. K., a 56-year-old white man, was admitted to the Jewish Hospital of Cincinnati on July 24, 1956, following an automobile accident on the preceding day in which he had sustained an anterior chest injury and fracture of the left tibia. He had been observed elsewhere and had seemed at first to be quite comfortable. In the ensuing hours, however, he had developed increasing difficulty breathing, and when finally transferred to this hospital was in extremis from respiratory insufficiency. Examination revealed marked cyanosis and dyspnea, and striking paradoxical motion of the anterior chest. The lungs were filled with secretions. X-ray studies revealed marked gastric dilatation, and a haziness in the right lower chest attributed to fluid.

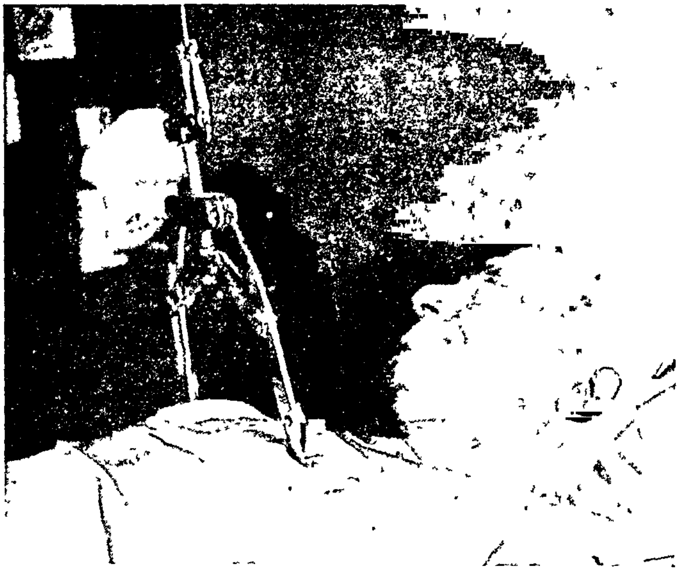

Fig. 4.—Photograph of the apparatus in use

The patient was taken immediately to surgery with a diagnosis of anteriorly crushed chest. A Levine tube was passed and the gastric dilatation relieved. An endotracheal tube was passed and the patient was lightly anesthetized with Pentothal sodium. One hundred per cent oxygen was administered, and copious bronchial secretions were aspirated. With the patient under respiratory control, following sterile preparation and draping, a flexible Kirschner wire was passed beneath the sternum according to the method just described. The incision was closed, and the ends of the wire were attached to a Kirschner wire spreader (Fig. 4). Respiration improved immediately with the application of traction. A complementary tracheotomy was then performed. The patient returned to his bed markedly improved.

Convalescence was uneventful. The severe wet lung present on admission cleared rapidly. The patient was treated with intravenous fluids and antibiotics, and was maintained on nasogastric suction for 2 days. Twenty pounds of traction were applied at first, and gradually reduced during the progress of the convalescence. The Kirschner wire was removed on Aug. 14, 1956, 21 days after operation, with the chest remaining completely stable. An interlobar hematoma of considerable size was present on the right side and was treated conservatively, with subsequent complete resolution. The tibial fracture healed satisfactorily following closed reduction. The patient has remained well following discharge from the hospital.

SUMMARY

Crush injuries of the chest are a particularly devastating type of injury, and lead rapidly to respiratory insufficiency because of (1) paradoxical respiration, (2) shallow rapid breathing, (3) inefficient cough, (4) accumulation of secretions, (5) paralytic ileus, and (6) cardiovascular embarrassment These mechanisms are directly related to the loss of integrity of the thoracic cage Immediate restoration of that integrity is essential This is usually best accomplished by skeletal traction An improved technique for skeletal traction in anterior crushed chest injuries is presented, involving the passage of a Kirschner wire beneath the sternum, the attachment of a Kirschner wire spreader bow to the ends of the wire, and the application of traction through the entire thickness of the sternum through the yoke so formed

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INTRAMURAL ABSCESSES OF THE ESOPHAGUS: A COMPLICATION OF FOREIGN BODIES

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ENDOSCOPISTS have reported drainage of acute localized phlegmons of the esophagus. Apparently these cases are rare since relatively few have been recorded. Experience with an intramural abscess of the esophagus, which clinically simulated a neoplasm and was treated by subtotal esophagectomy, aroused interest in the subject.

A review of the literature disclosed that previously reported parietal abscesses of the esophagus involved the presence of foreign bodies. This significant relationship is emphasized by the following report.

CASE REPORT

Miss K. O., a 56-year-old secretary, was admitted to the hospital on Nov. 25, 1957, with the complaint of retrosternal pain of 24 hours' duration. The previous day a constant, nonradiating retrosternal pain developed after the patient, who seldom ate meat, had a portion of a pork chop. The pain was markedly accentuated by swallowing but not by exertion or deep breathing. It was unrelieved by coughing or change of position. Patient stated that after the onset of the pain she had choking sensations which continued until the forenoon of the day of admission. At that time a large amount of thick, brown-colored, fluid-like material appeared in her throat. It did not result from a cough. Patient was relieved but was weak after this incident. She also reported some choking sensations which had occurred 4 to 5 months previously. There were no other symptoms related to the thoracic organs. There had been no loss of weight; her usual weight varied between 36.3 and 40.9 Kg.

There had been no previous serious illnesses or operations. She had been treated earlier in the year for an ''infected nose'' by an otolaryngologist. In January, 1953, patient had been hospitalized for swelling of the face and ankles due to secondary anemia and malnutrition. In August, 1956, she had been rehospitalized for a dull, intermittent pain in the left upper quadrant of the abdomen and left lower chest. Laboratory and roentgenologic studies resulted in the diagnoses of atropic gastritis and mild malnutrition. After fluoroscopy with a barium meal, the esophagus was reported normal. A history suggestive of sinusitis was elicited.

At physical examination the temperature was 36.8° C.; pulse, 78; respiration, 18; blood pressure 140/70 mm. Hg. The nasal and pharyngeal mucosae were injected and an apical systolic murmur was heard. The blood counts, urinalysis, and serological and blood chemistry determinations were essentially normal. The albumin/globulin ratio was 1.5:1. The corrected sedimentation rate was 30 mm. An electrocardiogram was normal. A thoracic roentgenogram made on November 26 revealed bilateral apical pleural thickening of a moderate degree and a few fibrotic strands in the left infraclavicular area. The heart was increased in size

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(17 per cent by measurement). There were mild sclerotic and degenerative changes in the thoracic aorta. A liquid barium esophagogram on the same day demonstrated almost complete obstruction at the junction of the middle and distal thirds of the esophagus; a very small amount of barium escaped past a filling defect which measured 5 cm. in length and appeared to be within the lumen. A slight dilatation of the esophagus was present, immediately proximal to the filling defect (Fig. 1).

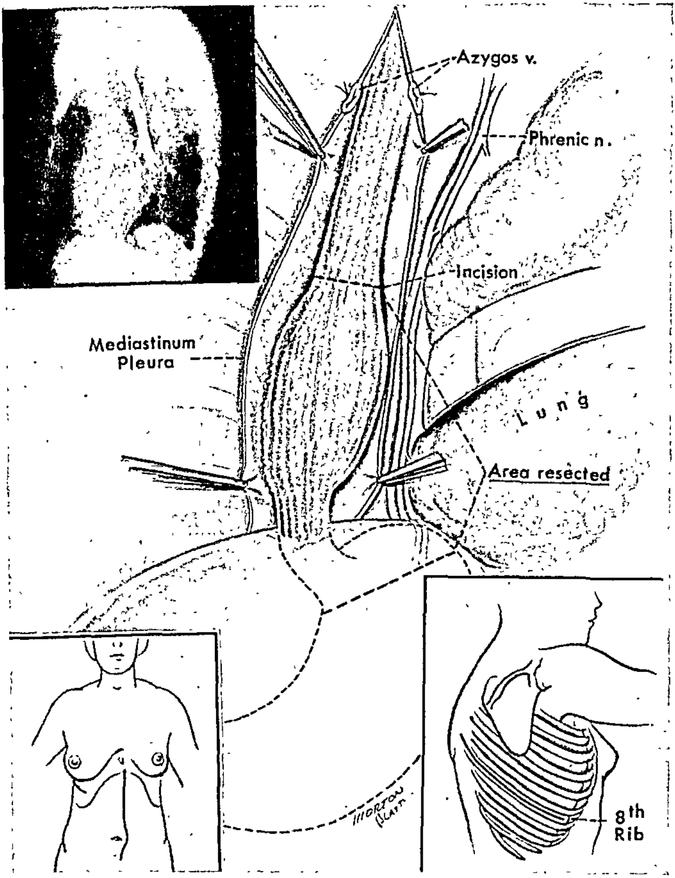


Fig. 1.—Artist's diagrammatic representation of lesion at the time of surgery, with preoperative roentgenogram.

Course in the Hospital.—On November 27 at esophagoscopy a foreign body (gray-colored bolus of food) was seen and removed from the middle of the esophagus. Distal to this site the normal-appearing mucosa bulged into the lumen, especially from the right side.

The lumen was thereby so narrowed that the esophagoscope was not advanced further. A biopsy showed normal esophageal mucosa. The foreign body was reported to be partially digested material of plant and animal origin; the latter included a small fragment of bone. The esophagogram was repeated on November 30, at which time an obstruction, almost complete, was again seen at the level of the eighth thoracic vertebra. An intraluminal-type defect was noted, with very little barium passing beyond the area. The roentgenologist concluded that a neoplasm of the esophagus was present. Intravenous fluids were given daily preoperatively.

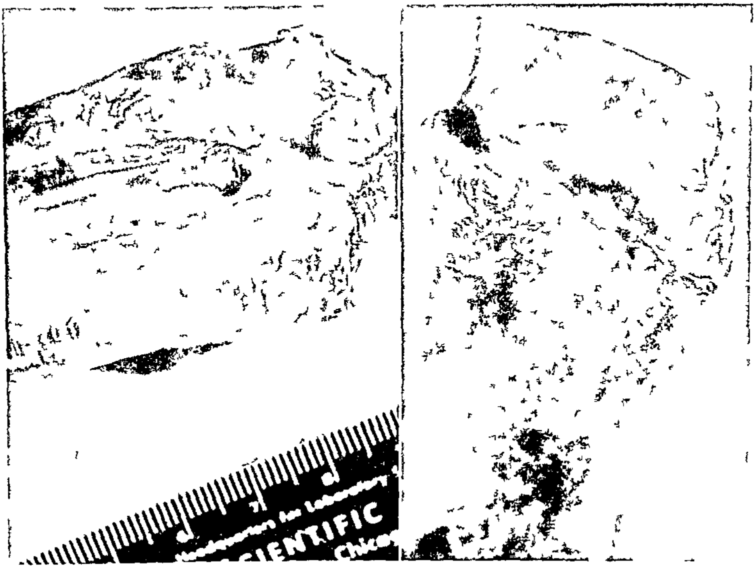
On December 2, a right thoracotomy revealed an 8 cm. cylindrical, smooth, firm mass in the esophagus below the arch of the aorta (Fig. 1). Its pink posterior surface was flecked with yellow. The mass was continuous above and below with normal-appearing esophagus. After the azygos vein was ligated and divided, the mass and distal esophagus was freed with ligation of vessels from the aorta and hilar areas. A small amount of granulation tissue was present in the posterior mediastinum adjoining the esophageal mass. The patient was then moved to a semi-supine position, and the peritoneal cavity was opened by a left paramedian incision. The stomach was mobilized by separation of the gastrohepatic and gastrocolic ligaments, with division of the vasa brevia artery, the left gastric artery, and the left gastro epiploic artery at its origin. The coronary ligament of the left lobe of the liver was divided, the esophagus freed from the hiatus, and the right crus of the diaphragm divided. A Heineke-Mikulicz pyloroplasty was then performed. The esophageal hiatus was enlarged to permit the introduction of three fingers. The liberated stomach was then pushed and simultaneously pulled up into the thorax through the enlarged esophageal hiatus. The abdominal incision was then closed. The proximal portion of the stomach was transected and the distal end closed. The sophagus was transected proximal to the tumor mass. The latter, plus the distal sophagus and gastric cardia, were removed as one specimen. An esophagogastrostomy ras then performed at the level of the sixth thoracic vertebra, and the stomach was utured to the mediastinum and esophageal hiatus. Two intercostal drainage tubes were laced in the right pleural space, and the thoracic incision was closed in layers. The atient's status throughout the procedure was exceptionally good; she left the operating room in satisfactory condition.

The surgical specimen was submitted to the Pathology Department without any attempt to incise or explore it. The pathologic report can be summarized as follows: The specimen consisted of the distal portion of the esophagus and the attached cuff of the fundus of the stomach. After sectioning, an irregularly shaped superficial ulcer, 2.0 by 0.5 cm., was seen in the mucosa, with its longer dimension along the axis of the esophagus. This was located 1 cm. below the superior edge of the resection and extended only through the mucosa and submucosa. The otherwise intact mucosa had a bluish-gray, smooth, glistening surface. Within the wall of the esophagus was a firm mass, measuring 7.0 by 3.0 by 1.2 cm. Cut section through this mass (Fig. 2) revealed smooth, glistening gray and tan surfaces, in the center of which was a small cavity (0.4 cm. in diameter) filled with purulent material. The ulcer was found to be connected to the abscess by a pin-point sinus tract.

Microscopic sections revealed an ulcer extending through the mucosa into the submucosa. The base of the ulcer was covered by many polymorphonuclear neutrophils. Beneath was a narrow tract of necrotic tissue, heavily infiltrated by polymorphonuclear neutrophils. This, in turn, was continuous with an abscess cavity containing many polymorphonuclear neutrophils and necrotic tissue. There was a suggestion of foreign material. At the margins of the ulcer and of the abscess, there was actively proliferating granulation tissue infiltrated by moderate numbers of lymphocytes and polymorphonuclear neutrophils. This tissue formed the outer margin of the specimen. The smooth muscle of the muscularis showed marked degeneration in the zone surrounding the abscess. A few foreign body giant cells were noted in the submucosa adjacent to the ulcer. There was a diffuse infiltration by polymorphonuclear neutrophils and lymphocytes of the muscularis about the lesion In one section a space lined by a thin layer of condensed hyaline like material was continuous with the abscess cavity The surrounding tissue in some areas was infiltrated with small foci of polymorphonuclear neutrophils

Diagnosis—(1) Intramural abscess of the esophagus, (2) ulcer of esophagus, superficial, subacute

The Chief Pathologist was consulted about the report of the specimen He stated that the abscess was essentially an acute process and not over 2 weeks old Inasmuch as the granulomatous reaction was minimal it could not be called a granuloma There was no evidence to suggest that the ulcer was of the peptic type or that a diverticulum had been present in the area of the lesion



A B

Fig 2—*A* Specimen opened demonstrating thickened esophageal wall and small ulcer with some mucopurulent material present in it. *B* Wall of specimen sectioned showing the thick wall of the abscess

Postoperatively, the patient's recovery was slow, but progressive Some pneumonitis developed in the left upper lobe and then cleared A roentgenologic study made on December 23 demonstrated retention of barium in the thoracic stomach after 3 hours On January 30, only a small residual of barium remained in the stomach when the test was repeated

It was necessary to treat a painful calcified bursitis of the right wrist as well as a painful left hip before the patient was discharged from the hospital on February 15

Dr F C Murphy continued to see the patient after she left the hospital On Nov 12, 1958, she reported to the writer that there was an occasional pain in the mid epigastrium an hour or more after eating soft regular food Her weight had been 31 4 Kg in the summer, but at that time was 36 3 Kg (height,

TABLE I. CASES OF INTRAMURAL ABSCESS OF THE ESOPHAGUS

CASE NO.	AGE	SEX	DURATION	ETIOLOGY	LEVEL	CLINICAL COURSE	AUTHOR
1	62	F	4 da.	Chicken bone	C^7 vert.	F.B.* removed; abscess drained; satisfactory x-ray in 9 days	Vistreich[13]
2	49	M	3 da.	Fish bone	18 cm.	F.B. removed; abscess drained; well in 3 days	Kramer[7]
3	49	M	10 da.	Fish bone	16 cm.	F.B. not seen; abscess drained; well in 2 days	Kramer[7]
4	?	?	8 wk.	Beef bone	?	Abscess drained; F.B. removed later; healed satisfactorily	Barker[3]
5	3	?	6 wk.	Coin (six pence)	12 cm.	F.B. removed; abscess drained; satisfactory x-ray in 3 weeks	Barker[2]
6	70	M	3 da.	Pork steak bone	C^6 vert.	F.B. removed after rupture of abscess in a diabetic patient	Schwartz[11]
7	26	M	4 da.	Denture	C^6 vert.	F.B. removed; abscess resolved	Matheson[8]
8	67	F	4 da.	Fish bone	21 cm.	Abscess drained; no F.B. seen; well in 4 days	Handke and Bade[6]
9	45	F	3 da.	Fish bone	19-20 cm.	Abscess drained; no F.B. seen; mediastinotomy later	Alpin[1]
10	45	F	4 da.	Lamb bone	15-16 cm.	Abscess drained; F.B. passed; well in 4 days	Alpin[1]
11	8	M	8 da.	Calf bone	12-14 cm.	Abscess drained; no F.B. found; well in 8 days	Alpin[1]
12	24	M	5 da.	F.B. with food	30 cm.	Abscess drained; stricture resulted, bougienage required	Clark[4]
13	?	M	3 da.	Bone	C^7 vert.	F.B. removed; later abscess drained	Robinson[10]

*Foreign body.

164.5 cm.). She stated that she had returned to her full-time duties as secretary on April 21. On May 6, 1959, the patient reported that she weighed 38 Kg. and had not been absent from work in over a year

DISCUSSION

Only a few cases of acute localized phlegmons of the esophagus have been reported. According to Graham, Singer, and Ballon,[5] von Hacker was the first to cure a patient with a circumscribed phlegmon of the esophagus by esophagoscopically removing the bone which caused the lesion. Handke and Bade[6] cited Seiffert as the first to describe the incision of an esophageal abscess via the esophagoscope. Graham and his associates reported Guisez as curing 5 patients who had almost complete stenosis of the esophagus because of marked bulging of the esophageal wall due to abscess formations. Kramer[7] stated that Guisez treated 8 patients with one death (patient was first seen when in extremis). Apparently no ill effects or stenosis occurred. Albrecht and Hertzog, also cited by Graham, obtained good results using the same techniques. One of 3 patients, treated similarly by Gottstein, died of mediastinitis on the eighth day.

The literature revealed, in addition to those already mentioned, 13 cases of acute esophageal abscesses (Table I). These occurred in patients from 3 years of age to 67, with nearly an equal number of males and females. It is significant that the abscesses developed, and were large enough to cause obstruction, in a number of the cases in less than 5 days. The etiological agent in all cases was the incomplete swallowing of a foreign body, usually fish or meat bones, but a coin (six pence) and a denture were also causative factors. The abscesses were located at varying levels in the esophagus, but were mainly between 12 and 30 cm. from the upper incisor teeth. In some cases the foreign body was not found. When seen, it was removed. Drainage of the abscesses was usually accomplished with the aid of an esophagoscope. Stenosis developed in 1 case (at 30 cm.) and bougienage was required subsequently. In 2 of the cases, the periesophageal tissues were probably involved, but an attempt has been made to cite only localized phlegmons. A collar mediastinotomy was performed in a complicated case reported by Alpin.[1]

Terracol and Sweet[12] have in their monograph a brief, well-written chapter including abscesses of the esophagus. In the bibliography, a case of traumatic abscess reported by Nys[9] is given.

In the differential diagnosis of obstructive lesions of the esophagus, a parietal abscess should be considered, especially when a foreign body has been present. As to definitive treatment, drainage, utilizing an esophagoscope, is a more conservative type of surgical procedure. However, subsequent bougienage may be required for cicatricial stenosis of the esophagus. In advanced lesions, the wall of the esophagus might be destroyed to the extent that resection is indicated.

The possibility of an intramural or parietal abscess of the esophagus was not considered preoperatively, or during surgery, in the case just described. The patient was afebrile and had a normal total and differential leukocyte count on admission. The esophagogram suggested a neoplasm, as was true in one of Kramer's cases (Case No. 3, Table I). Undoubtedly a stricture would have resulted if a drainage procedure had been done at surgery. Thus, resection prevented subsequent need for bougienage. This patient probably would not have tolerated such procedures repeatedly. A drainage operation at the time of thoracotomy is not without other complications than stricture. Mediastinal suppuration, with its ramifications, is one of several possibilities. It is fortunate that the abscess did not perforate into the mediastinum to any extent.

The mucosa of the esophagus is apparently easily injured by foreign bodies. Bacteria then have a portal of entry to the underlying tissues, which have very little resistance to contamination, and infection and suppuration develop rapidly.

The present case also illustrates the need for a correct histologic diagnosis before refusing, or failing to recommend, surgery in patients with obstructive lesions of the esophagus. Roentgenologic examinations are helpful but may be misleading.

SUMMARY

An intramural abscess of the esophagus has been described. The benign condition simulated a neoplasm roentgenologically before surgery and was treated successfully by resection. The reported cases of acute localized phlegmons of the esophagus have been summarized and their association with foreign bodies has been emphasized.

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A CASE OF PURE ENDOBRONCHIAL CHONDROMA

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THE PURPOSE of this paper is to report a case of a pure chondroma of endobronchial origin, occurring in a middle aged woman These tumors arising from this site are extremely rare and only a few cases have been reported in the literature

Almost all these cartilaginous tumors have been called "hamartomas," a term which originated from Albrecht,[1] in 1904, who stated that "hamartomas are tumor like malformations in which occur only an abnormal mixing of the normal components of the organ The abnormality may take the form of a change in quantity, arrangement and degree of differentiation, or may comprise all three The deduction to be drawn from histologic examination of these formations is that they have originated in an abnormal mixing of the elements or from disturbances of their development" The term as originally coined by Albrecht was applied to such tumors of the liver

CASE REPORT

A 55 year old white woman was admitted to St John's Riverside Hospital on May 12, 1958, with a chief complaint of fever and cough The patient had been in good health until approximately 10 days prior to admission, when she noted the onset of fever accompanied by muscular aching and cough The fever was intermittent with daily temperature rises The cough was productive of a moderate amount of tan colored sputum which occasionally was blood streaked The patient was treated at home by a physician with supportive therapy and, when she failed to improve, hospitalization was advised

A review of her past history revealed that she had had several similar episodes within the previous 6 months The patient had no wheezing in the chest but had mild dyspnea on exertion She complained of pain in the right upper chest region anteriorly and laterally which was pleuritic in nature Her systemic review was noncontributory to the present illness

The patient had had pleurisy in the right chest approximately 10 years prior to this admission A tonsillectomy was performed at the age of 18 and she had the usual childhood diseases She was a relatively heavy smoker, admitting to more than one pack per day She had no history of allergy Positive physical findings were limited to the chest where there was evidence of decreased breath sounds in the right upper lung field anteriorly and posteriorly with dullness and a positive cough sign

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Initial treatment consisted of erythromycin, expectorants, aspirin, and sedation. An electrocardiogram was within normal limits. A chest roentgenogram (Fig. 1) revealed flocculant mottled infiltrate which involved the posterior segment of the right upper lobe. A temperature of 103° F. occurred on the first day, with return to normal in 5 days. The cough, however, persisted, as did the pain in the chest. Six days following admission repeat x-ray studies (Fig. 2) showed further atelectatic changes in the right upper lobe region and neoplasm was suspected.

Bronchoscopy was performed on January 24 under local anesthesia and a mass was found which occluded the right upper lobe orifice completely. The mass was grayish-pink and appeared to be fungating. A biopsy showed bronchial mucosa with hyaline cartilage beneath the mucosa. It was thought that the biopsy had been inadequate.

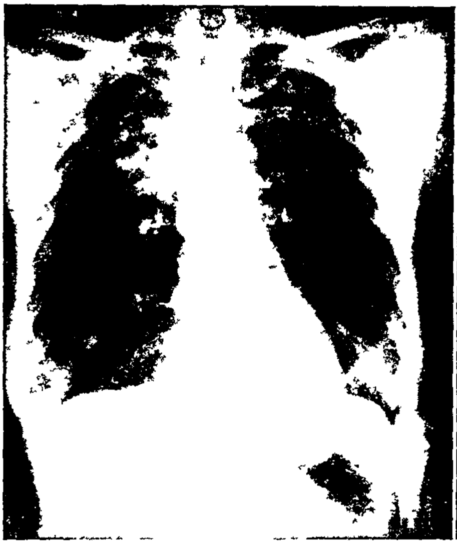

Fig. 1

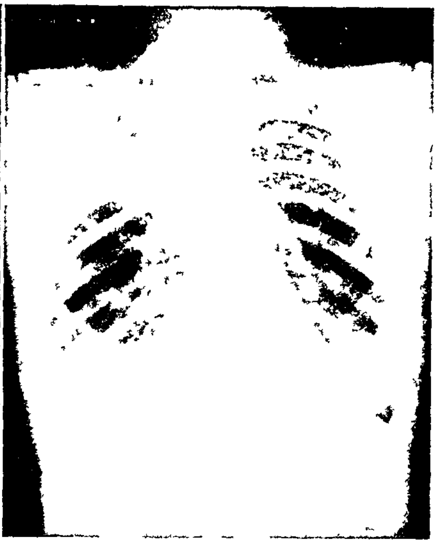

Fig 2

Fig. 1 —Roentgenogram taken on admission discloses a flocculant mottled infiltrate involving a segment of right upper lobe

Fig. 2.—Roentgenogram made 6 days later discloses atelectatic changes in the right upper lobe region with the possibility of neoplasm as suggested by the roentgenologist.

Because of the clinical diagnosis of bronchogenic carcinoma, an exploratory thoracotomy was performed on May 27, 1958. Due to the absence of an absolute pathologic diagnosis, the main right upper lobe bronchus was opened posteriorly and the mass was again noted. Several punch biopsies were taken and frozen section examination again revealed only cartilage. The diagnosis of benign chondroma was made and the incision in the bronchus was extended into the apical segmental bronchus where it was found that the mass was a chondroma on a very small pedicle originating in the right upper lobe apical bronchial segment. The pedicle was excised with an ovoid incision through the mucosa. The area from which the tumor had arisen was curetted with a small curette. The bronchus was closed with interrupted 4-0 silk sutures and a pedicle graft of pleura was placed over the incision in the bronchus.

The patient made a completely uneventful convalescence, with complete expansion of the right upper lobe. She was discharged on the ninth postoperative day in good condition.

The pathologic report was as follows: the gross specimen consisted of an irregular, small, whitish, firm chondroma, glistening upon sectioning and measuring 0.8 by 0.6 by 0.6 cm.

Microsections showed a typical chondroma partially lined by the normal mucosa of the bronchus. The cartilage was composed of a uniform transluscent matrix with evenly situated oval lacunae containing small cartilaginous cells which were adult in type. There was a complete absence of other types of tissues which might warrant classification of this tumor as a hamartoma. Malignancy was absent.

DISCUSSION

According to McDonald, Harrington, and Clagett,[2] it cannot be denied that pure chondromas of the lung occur, although they have had no experience with them as such. These authors indicate that cartilaginous tumors in the lungs are occasionally referred to as chondromas, when the other elements, such as epithelium, fat, and smooth muscle, are incorporated in the tumor. These are not true chondromas.

According to Rubin and Beckman,[3] location of a chondromatous hamartoma in a bronchus is uncommon. They reported the fourteenth case of this type and they were unable to find a single pure chondroma in 8,800 necropsies reviewed. Because of the close relationship of pure chondromas of the bronchus and hamartomas, these tumors, for convenience and symptomatology as well as prognosis, should be considered as similar tumors.

In an article by Nissen and his associates,[4] cartilaginous tumors of the lungs are frequently encountered at autopsy. They are usually peripherally located, are of hamartomatous nature, and are not clinically significant. Cartilaginous tumors arising from the large bronchi are of clinical importance because they give rise to signs and symptoms which may be easily interpreted as due to carcinoma but are amenable to curative surgical procedures. These authors found only 20 cases in reviewing the medical literature.

According to Young and his associates,[5] endobronchial hamartomas have occasionally been removed through the bronchoscope and none has been known to recur. They often produce recurrent pneumonitis and atelectasis and make it desirable to remove the involved segment. The most frequent symptoms have been cough and hemoptysis. The roentgenograms in the cases of Young were not diagnostic of bronchial tumors. A review of the literature by these same authors disclosed 24 cases of endobronchial hamartomas. Of the 24 cases reported, 13 arose in the right lung and 11 in the left lung. Seven of the tumors were incidental findings at autopsy and the other 17 produced symptoms. There has been no instance of a bronchial chondroma becoming malignant.

In a 1958 publication, Hodges[6] found that in 200 reported cases of hamartomas of the lungs, the tumor was endobronchial in 33 and in the lung parenchyma in the remainder.

SUMMARY

This is the report of a middle-aged white woman who was admitted to the hospital mainly for cough and fever. The symptoms and signs, including x-ray interpretations, were those of a neoplasm, probably carcinoma. However, upon opening the bronchus at thoracotomy, a pedunculated firm tumor was found

completely obstructing the lumen of the right upper lobe. Frozen and paraffin sections disclosed it to be a pure chondroma. On the ninth day following removal of the growth, there was complete expansion of the right upper lobe and the patient was becoming symptom free.

This case seemed to follow the pattern of most of the cartilaginous endobronchial tumors reported in the literature, with obstructive bronchial signs followed by atelectasis, and complete cure following the removal of the tumor.

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ACQUIRED TRACHEOCELE: AN UNUSUAL LESION

Surgical Resection in a Case Associated With Trachiectasis and Bronchiectasis

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Among the benign conditions affecting the tracheobronchial tree, diverticulum, or tracheocele, represents one of the more uncommon. Essentially, this lesion consists of an out-pouching, or sac, formed by membranous trachea at its junction with the cartilagenous rings (the cornu). The more common congenital variety is usually small and narrow-mouthed, probably representing a supernumerary bud which has failed to become isolated as a bronchogenic cyst. Typically, these occur about 4 to 5 cm. below the true vocal cords, most often present at the right cornu, are clinically silent, and sometimes multiple.

The acquired variety, on the other hand, is usually wide-mouthed, tends to be larger in size, may occur at any level, and often produces esophageal compression. Chronic infection in glands of the posterior tracheal wall with progressive destruction of elastic tissue has been postulated as its etiology. Trachiectasis and/or bronchiectasis may be associated and secondary to it. Indeed, the signifiance of such a diverticulum resides not only in its ability to produce cough, but more importantly in its acting as a reservior for secretions which may result in chronic reinfection of the tracheobronchial tree.

Although described by Rokitansky[1] over 100 years ago, relatively few cases of tracheocele have been reported. The great majority of these has been of the congenital type, incidentally noted at necropsy or bronchographic examination. Drymalski,[2] Mackinnon,[3] Goldman,[4] and others[5, 6] have reviewed the various aspects of this lesion and presented cases. In 1944, Addington and coworkers[7] reported an acquired tracheal diverticulum in a 32-year-old man who had complained of cough, dyspnea, and wheeze for 8 years. This was a wide-mouthed sac demonstrated at bronchoscopic examination, produced esophageal compression, and was accompanied by basilar bronchiectasis.

Three surgical cases have been recorded in which tracheocelectomy was performed. In 1943, Christmann and Albano[8] described cervical excision of a plum-sized sac communicating between the second and third tracheal rings. During the previous 15 years it had been intermittently palpable in the right

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supraclavicular fossa and had become the site of recurrent infection with purulent sputum. In 1950, Mathey and Lemoine[9] operated upon a 16-year-old girl who was found to have a congenital tracheoesophageal fistula (without atresia) as well as a congenital tracheocele. The former entered the trachea 3 cm. above the main carina and was divided and closed. The subjacent tracheocele was excised. In 1951, Clagett[10] operated upon a 52-year-old man who complained of long-standing productive cough. Utilizing a sternum-splitting incision, he resected an acquired diverticulum of the trachea presenting from the left cornu just below the clavicle. Complimentary tracheostomy was performed to reduce the mean intratracheal pressure.

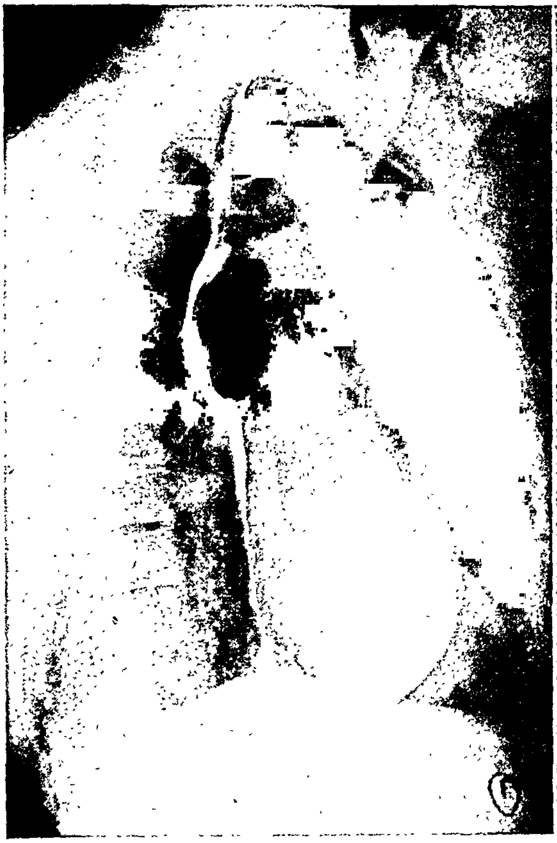

Fig. 1.

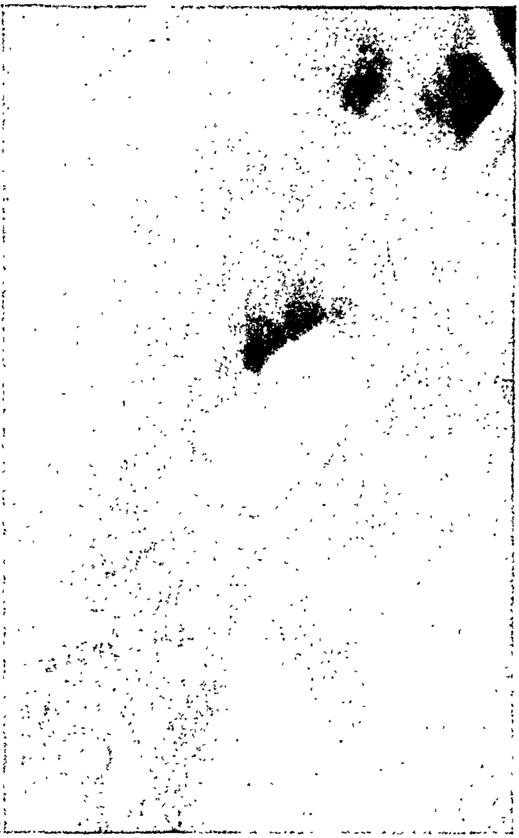

Fig. 2.

Fig. 1.—Barium esophagram in right anterior oblique view which shows displacement of esophgus at level of aortic arch.

Fig. 2.—Spot film of lower trachea with patient recumbent, taken following instillation of oily Dionosil. Note pooling in diverticulum.

CASE REPORT

R. B., a 59-year-old widow, was seen in consultation because of a chronic recurrent productive cough of 28 years' duration. Prior to age 30, she had enjoyed excellent health with no symptoms referable to the respiratory system. In 1931, about 1 year prior to undergoing a uterine suspension, she had noted the onset of a dry cough, the cause of which was unexplained. Very shortly following this operation, the cough increased in severity and became productive of mucopurulent sputum. During the ensuing several years the cough was almost constantly present, and severe paroxysms frequently induced vomiting and became quite incapacitating. She sought medical consultations, but repeated physical examinations and chest roentgenograms were said to be unremarkable. Her "chronic bronchitis" was treated with a multiplicity of antitussives, sedatives, antihistamines, expectorants, inhalants, and chemotherapeutic agents with only partial or transient relief. In 1948 a severe episode of pneumonitis and pleurisy occurred.

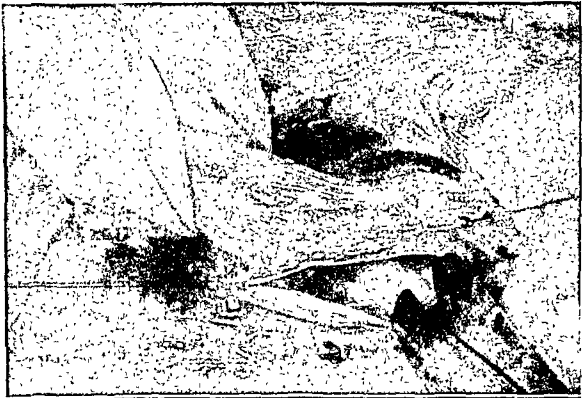

Fig. 3.

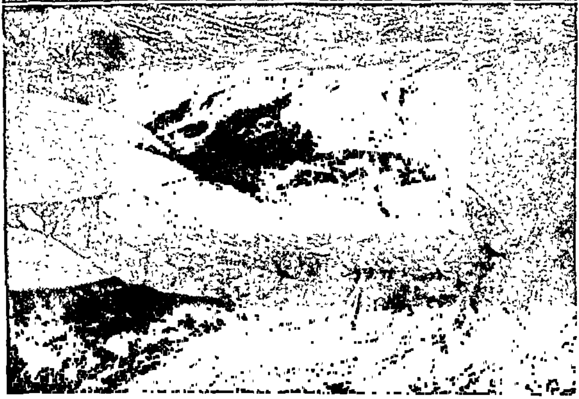

Fig. 4.

Fig. 3.—Photograph at operation with tracheocele open. Tape surrounds the left mainstem bronchus. Note descending aortic arch at right and below.

Fig. 4.—Same view as Fig. 3 which shows closure of membranous trachea. Vagus and recurrent nerves are seen above. Note esophagus below between bronchus and aorta.

In 1956, while vacationing in Florida, an extraordinarily severe episode of coughing occurred, and she was hospitalized. Chest roentgenograms were said to be normal. Bronchoscopic examination was performed and reported to reveal a "very unusual condition" characterized by an "impaction of glue-like secretion in the lower trachea." This was aspirated, and the cough tended to subside almost completely for the ensuing 2½ years. However, in March, 1959, it recurred, again becoming productive of thick sputum. She was admitted for study.

Physical examination showed a well-nourished woman with no evidence of dyspnea, cyanosis, or clubbing. There was a hoarse, low-pitched, rattling cough of a very unusual character. Auscultation revealed a loud coarse wheeze over the anterior thorax with maximal intensity over the upper sternum. On inspiration this sounded like swirling eddy currents of air.

Hematologic studies and urinalysis were normal. Sputum smears showed many leukocytes and some bacteria; all cultures showed no growth. An electrocardiogram was normal.

Bronchoscopic examination revealed a cylindrically dilated and somewhat bulbous trachea. Just above the main carina on the posterolateral wall a wide-mouthed orifice was observed communicating with a smooth-lined diverticular pouch. With inspiration the mobile sac wall ballooned out, and at expiration its dome partially prolapsed into tracheal lumen, vibrating against the wall of the orifice.

Conventional roentgenograms of the thorax showed a circumscribed oval radiolucency at the left tracheal border. An esophagram (Fig. 1) showed posterior displacement of the esophageal segment opposite the aortic arch. Tomograms in the coronal plane demonstrated the paratracheal radiolucency to be devoid of lung markings. Angiocardiography showed no abnormality of pulmonary vasculature. Bronchography under fluoroscopic control revealed the following information: with the patient semirecumbent, 4 c.c. of oily Dionosil was instilled by catheter into the mid-trachea and seen to pool in the diverticulum just above the main carina (Fig. 2). The head of the tilt table was then elevated, and the contrast material emptied into both bronchial trees. This occurred in the absence of any coughing; no esophageal dye was seen. The upright films showed moderate cylindrical bronchiectasis of the basilar segments in each lower lobe. Diffuse trachiectasis was also evident.

Left lateral thoracotomy was performed on April 7, 1959, under endotracheal anesthesia. The thin-walled diverticulum presented in the aortic window just under the arch and was dissected free of surrounding tissue. It was quite intimately adherent to the esophagus. The sac measured 3 by 2 by 1.5 cm. Traction sutures were placed, and it was momentarily opened for inspection (Fig. 3). A Satinsky clamp was placed across its base and proximal excision performed, closing the defect with two layers of the silk (Fig. 4). Postoperatively, the patient's course was entirely uneventful. Although still present 3 months later, her cough has become progressively less marked and less productive. The severe paroxysms are no longer present, and subjective improvement is striking.

Microscopic sections of the sac showed layers of membranous trachea with no inflammation.

COMMENT

In this patient the onset of symptoms after the age of 30 and the morphologic characteristics of the tracheocele strongly suggest the latter to have been an acquired lesion. The associated bronchiectasis and trachiectasis lessened our hope for a surgical cure of the cough; however, considerable mitigation of its severity has already occurred.

SUMMARY

The subject of congenital and acquired tracheoceles has been briefly reviewed. A case is reported of a 59-year-old widow with long-standing chronic cough of occult etiology. Excision of a tracheocele was performed with marked palliation.

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ABERRANT LEFT PULMONARY ARTERY

A Correctable Cause of Respiratory Obstruction

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INTRODUCTION

THE SURGICAL RELIEF of respiratory obstruction caused by vascular anomalies was started by Gross[1, 2] in 1945 with division of a double aortic arch. Interest since then has centered around correction of aortic arch anomalies. In the past 2 years we have encountered 3 cases of aberrant left pulmonary artery which caused respiratory obstruction. In these cases, the left pulmonary artery arose on the right of the mid-line and passed posteriorly and to the left between the trachea and esophagus to reach the left hilum (Fig. 1). Since, in 2 of our cases, the surgeon's failure to recognize the true nature of the abnormality led to an incorrect procedure, it seems desirable to call attention to this lesion.

The first case of aberrant left pulmonary artery associated with tracheobronchial obstruction was reported in 1938[3] and 16 years elapsed before the report of 2 additional cases[4, 5] in 1954. A total of 15 cases have now been reported (Table I). The fact that 11 of these have been reported from four clinics suggests that this anomaly is more common than previously appreciated.

CASE REPORTS

CASE I.—(Table I—Case XIII.) L. D., No. 8456, born May 14, 1956, died Sept. 22, 1956.

The patient, a white girl, was admitted to the Babies Hospital at the age of 7 weeks with a history of dyspnea since birth. There were wheezes in both lungs and marked stridor. Chest roentgenogram showed obstructive emphysema on the right with mediastinal shift to the left. No abnormalities were seen on direct laryngoscopy or esophagram. Bronchoscopy was not done.

At the age of 11 weeks, with a presumptive diagnosis of bronchogenic cyst, the right pleural cavity was opened. The right lung was found to be emphysematous, but no cyst or other abnormality causing bronchial obstruction was found. The mediastinum was not dissected.

Following operation, stridor and tachypnea persisted. A combined tracheo-esophagram showed marked indentation of the posterior trachea and anterior esophagus at the level of the carina, well visualized in the lateral view but poorly seen in the posteroanterior projection (Fig. 2).

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Two weeks later, the right chest was re opened and the mediastinum dissected A large blood vessel was found arising from the right pulmonary artery anterior to the innominate passing posteriorly over the origin of the right primary bronchus around the lateral aspect of the right of the trachea, and then medially to the left between the trachea and esophagus Its further course could not be identified The vessel was thought to be a right patent ductus

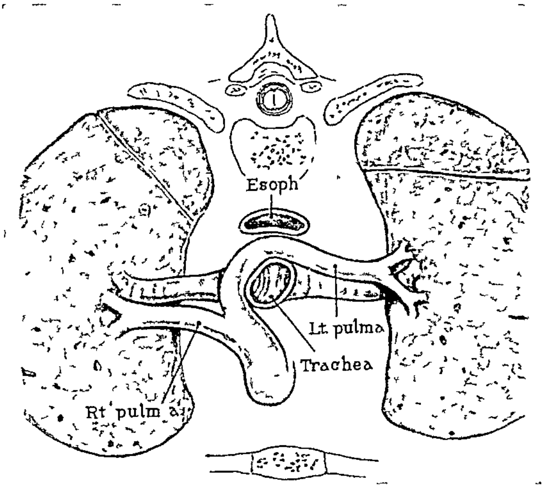
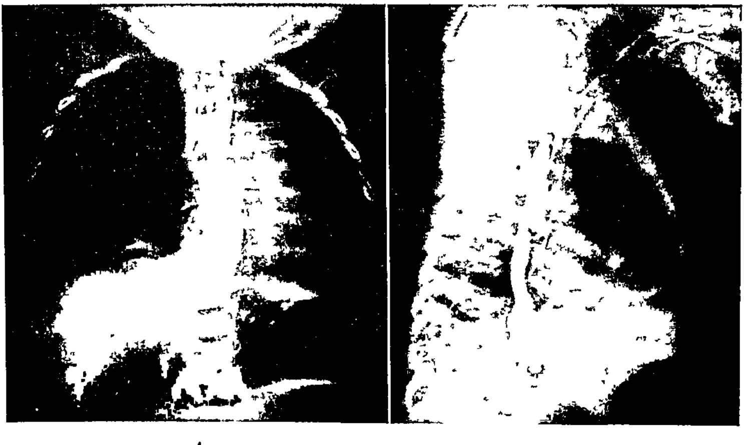


Fig 1—Diagrammatic representation of aberrant left pulmonary artery (cross section)


A

B

Fig 2—Case I A, Posteroanterior tracheo esophagram which fails to show the abnormality B, Lateral tracheo-esophagram demonstrating the aberrant left pulmonary artery

arteriosus. After 5 minutes of well-tolerated occlusion it was divided. The postoperative course was characterized by increasing respiratory distress, and death occurred 48 hours later. Postmortem examination revealed, in addition to the aberrant left pulmonary artery (Fig. 3) which had caused compression of the trachea and right main bronchus, the following pathologic features: (1) persistent left superior vena cava emptying into a large coronary sinus, (2) ostium secundum defect 8 mm. in length (slit-like), (3) anomalous branch of left pulmonary artery to right upper lobe, (4) anomalous tracheal cartilages: complete cartilaginous rings in the lower trachea and main bronchi, (5) high origin of right upper lobe bronchus (epiarterial), and (6) emphysema in the right upper lobe and atelectasis in the right middle and lower lobes.

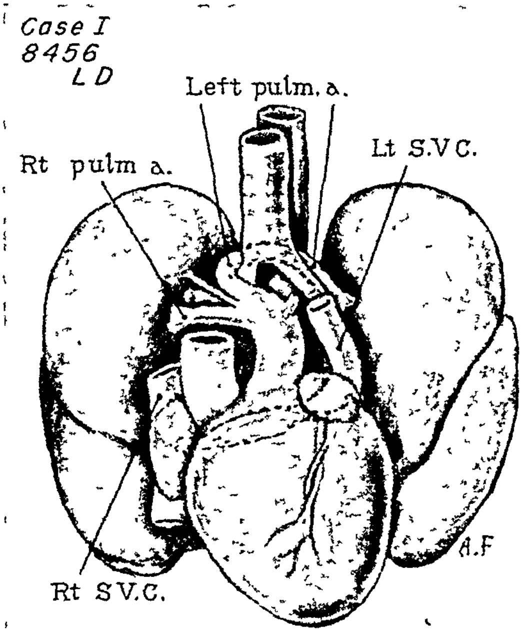


Fig. 3.—Case I (Table I—Case XIII).

Case II.—(Table I—Case XIV.) D. A. No. 8678, born Dec. 13, 1952, died Nov. 15, 1957.

The patient, a Negro girl, was first admitted to the Babies Hospital at the age of 2 weeks with a history of respiratory distress since birth. Stridor and moderate tachypnea had persisted with frequent exacerbations throughout her life. At the age of 6 weeks the diagnosis of congenital heart disease was made on the basis of a harsh systolic murmur, cyanosis, and an abnormal cardiac configuration on a chest roentgenogram. Cardiomegaly was progressive. An esophagram at the age of 8 months disclosed a right aortic arch without other evidence of esophageal compression.

Angiocardiography done at this time was interpreted as showing persistent truncus arteriosus. The course of the pulmonary arteries was not clear. Bronchoscopy and tracheobronchogram were not done. After repeated exacerbations of symptoms, she was admitted for the eighth time at the age of 4 years and 11 months in severe congestive heart failure and shock. Death occurred 4 hours later. Necropsy (Fig. 4) revealed in addition to the aberrant pulmonary artery: (1) tetralogy of Fallot with atresia of the pulmonary valve and high ventricular septal defect (1.3 cm.), (2) ostium secundum defect (0.8 by 1.5 cm.), (3) patent ductus arteriosus (1.2 cm. circumference), (4) peristent left superior vena cava entering the coronary sinus, (5) right aortic arch and anomalous origin of the right common carotid (right vertebral and right subclavian arteries), (6) singled-lobed left lung, (7) anomalous branch of the left pulmonary artery supplying the right upper lobe, and (8) hyperostosis of calvarium with compression of frontal lobes.

CASE III.—(Table I—Case XV.) N. F., No. 8888, born Oct. 19, 1958, died Dec. 24, 1958.
This infant was admitted to the Babies Hospital at the age of 8 weeks with a history of wheezing for 3 weeks. Physical examination revealed stridor, chest retraction, and slight cyanosis. Chest roentgenogram showed emphysema of the right lung. Esophagram disclosed anterior indentation at the level of the carina, best seen in the left anterior oblique view. The child's course was characterized by rapidly progressive respiratory distress. A tracheo-esophagram was done by the "gulp" technique (described later) which showed separation of the trachea and esophagus by an abnormal structure, well seen in the posteroanterior roentgenogram (Fig. 5, *A*). A left anterior oblique esophagram demonstrates the size of the vessel wall (Fig. 5, *B*). A presumptive diagnosis of bronchogenic cyst was made. At operation the right lung was found to be almost completely consolidated. An abnormal vessel was identified arising to the right of the mid line in the mediastinum, anterior to the trachea, passing to the right around the lateral and posterior aspects of the trachea, and then medially to the left, anterior to the esophagus. The possibility that this represented an aberrant left pulmonary artery was considered but aspiration of the vessel yielded bright red blood under arterial pressure. A diagnosis of double aortic arch was made. After occlusion for 5 minutes was well tolerated, the vessel was divided. Postoperatively, assisted respiration was required, and heart action ceased after 6 hours. Necropsy examination revealed, in addition to the aberrant pulmonary artery (Fig. 6) with compression and malacia of the right main-stem bronchus, the following pathologic features: (1) ostium secundum defect 5 by 11 mm. and fenestrated septum primum with its largest opening 4 by 6 mm., (2) patent ductus arteriosus, 7 mm. in length and 4 mm. in circumference, (3) anomalous tracheal cartilages (complete cartilaginous rings in the lower trachea and main bronchi), and (4) absence of gall bladder.

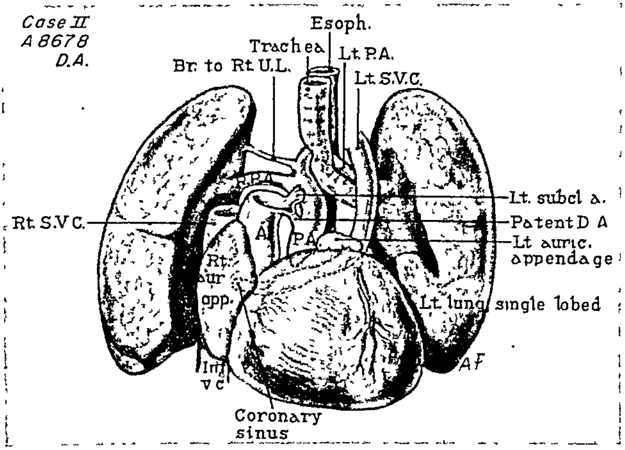
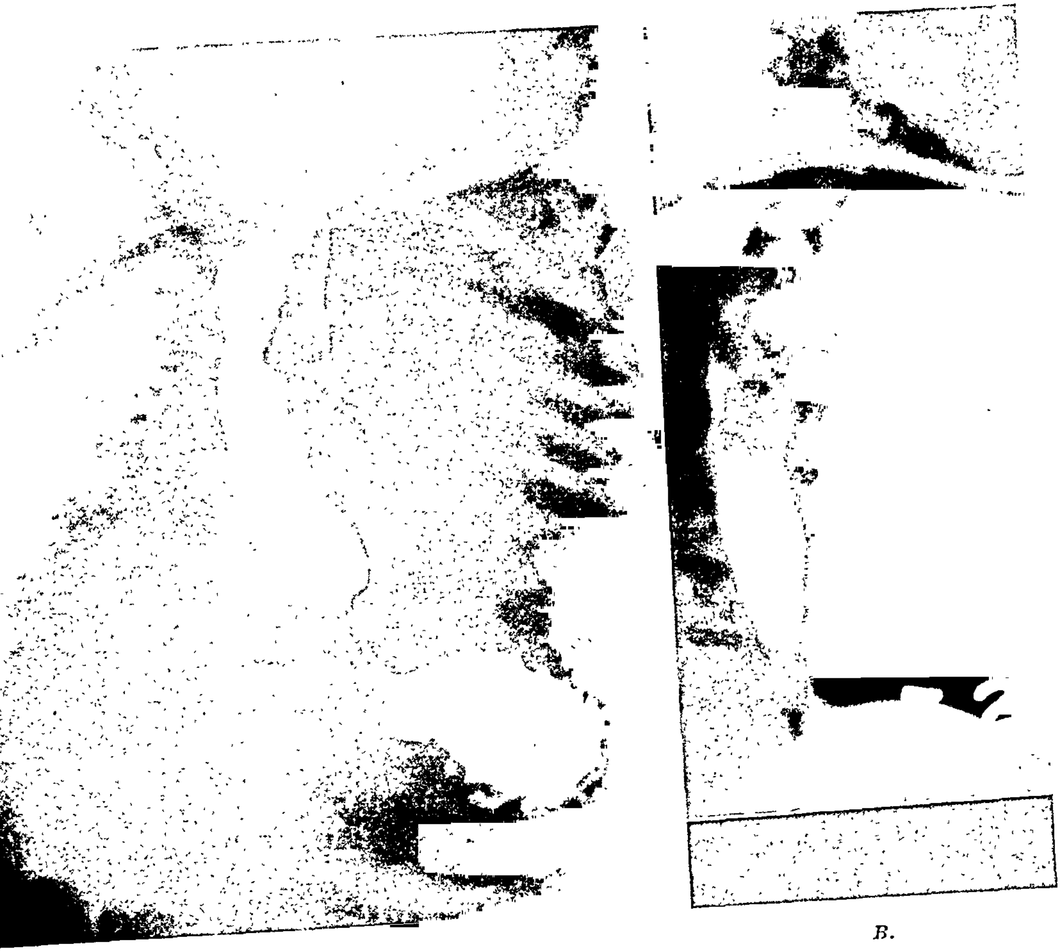


Fig. 4.—Case II (Table I—Case XIV).

DISCUSSION

The diagnosis of aberrant left pulmonary artery should be considered in all infants with persistent stridor. Symptoms of respiratory distress appeared in the first month of life in all but one reported case, with stridor generally noted



B.

A.

Fig. 5.—Case III. *A*, Posteroanterior tracheo-esophagram which demonstrates separation of the trachea and esophagus by the aberrant left pulmonary artery.
B, Left anterior oblique esophagram which shows esophageal indentation by the aberrant left pulmonary artery.

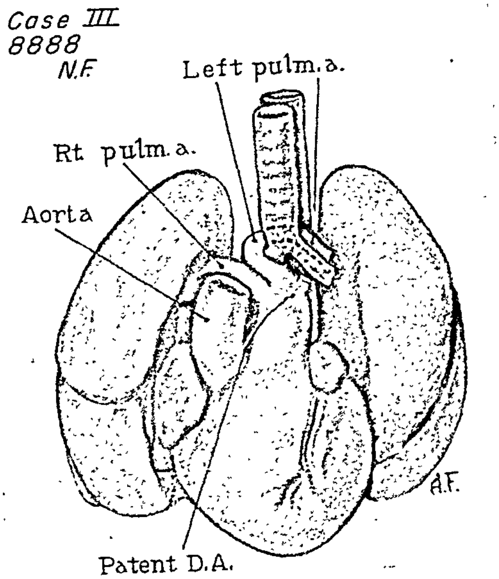


Fig. 6.—Case III (Table I—Case XV).

at birth or shortly afterward. In contrast to the clinical picture presented by most other vascular ring anomalies, symptoms of esophageal obstruction have not been noted. *Patients have presented with any or all of the following symptoms:* stridor, dyspnea, cyanosis, and repeated respiratory infections. The course is usually progressive with occasional lessening but never disappearance of symptoms. Physical findings may include stridor, retraction, tachypnea, wheezing, hyperresonance on the right with tracheal deviation to the left, and cyanosis. When pulmonary infection is superimposed, bilateral râles, rhonchi, and fever *may appear. This can obscure the primary factor of respiratory obstruction.*

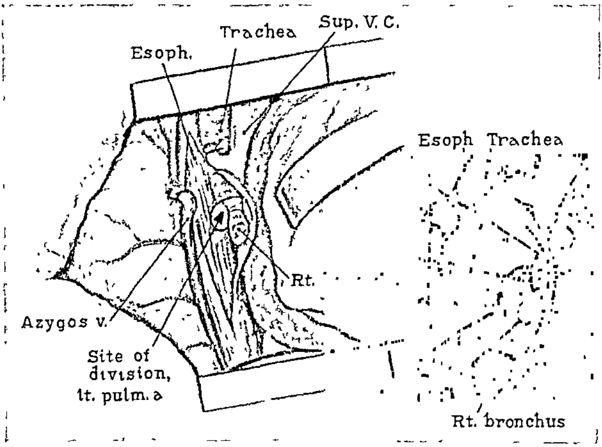


FIG 7—Surgical approach for correction of aberrant left pulmonary artery. Insert shows the divided left pulmonary artery being re-anastomosed after division and transplantation medial to the right main-stem bronchus.

Chest x-ray findings have been variable. The most common picture is that of emphysema of the right lung with mediastinal shift to the left. Lateral view may show narrowing of the lower trachea. Bronchoscopy has been consistently useful in demonstrating narrowing of the trachea or right main-stem bronchus. However, this procedure is hazardous in infancy and it is our belief that the diagnosis can be made conclusively by other techniques. Angiocardiography has been reported as diagnostic.[8] In Case II of the present series, the anomalous left pulmonary artery was not visualized by this technique because of the presence of a tetralogy of Fallot with atresia of the pulmonary valve.

In our experience, the most important diagnostic aid has been the combined tracheo-esophagram, utilizing the "gulp" technique. In this procedure, 5 to 10 c.c. of aqueous Dionosil is instilled into the posterior pharynx followed immediately by occlusion of the nose and mouth. This causes the patient to swallow

TABL

SE .	AUTHOR	SEX	AGE AT ONSET OF SYMPTOMS	DIAGNOSTIC TESTS		
				X-RAY CHEST	ESOPHAGRAM	BRONCHOSCOPY
	Scheid[3]	Male	7 mo.	Normal	—	Narrowing of lower trachea
	Welsh & Munro[4]	Male	2 wk.	Normal	Unsatisfactory study	—
.	Potts et al.[5]	Male	Birth	Emphysema rt. lung; left mediastinal shift	Normal	Extrinsic pressure on lower trachea and rt. main bronchus
	Morse & Gladding[6]	Male	Birth	Changing findings rt. lung; left mediastinal shift	—	Narrowing rt. mainstem bronchus
	Wittenborg et al.[7]	Male	4 da.	Diffuse emphysema; narrowing trachea	Posterior indentation; slight anterior indentation	Narrowing trachea just above carina
.		Male	Birth	Normal	—	—
I.	Hiller & Maclean[8]	Female	Birth	—	Anterior indentation of esophagram	—
II.		Male	?	—	Anterior indentation of esophagram	—
.		Female	Birth	—	Anterior indentation of esophagram	—
	Contro et al.[9]	Female	1 mo.	? Enlarged thymus	Anterior indentation esophagus	Moderate narrowing of distal trachea; collapsed rt. mainstem bronchus (performed on operating room table with chest open)
[.		Male	4 da.	Normal	—	

I

ANGIOCARDIOGRAM	AGE AT OPERATION	OPERATION	AGE AT DEATH	DIAGNOSIS ANTE MORTEM	ADDITIONAL FINDINGS AT AUTOPSY
—	—	None	10 mo.	No	Complete tracheal cartilagino rings; patent ductus arteriosus; ostium secundum def (1 by 1.5 cm.)
—	6 mo.	Anomaly appreciated at exploration; cardiac arrest before correction attempted	6 mo.	At operation	None mentioned
—	5 mo.	Anomalous left pulmonary artery divided and re-anastomosed to the left of the trachea; excellent result	—	Yes	—
—	1 mo.	Anomalous left pulmonary artery divided and re-anastomosed medial to the trachea; initial improvement with early recurrence of respiratory obstruction	1½ mo.	At operation	None
—	—	None	3 mo.	No	Aberrant right subclavian artery; persistent left superior vena cava to coronary sinus; hypoplasia left kidne partial malrotation on intestine; hemivertebrae
—	—	None	3 mo.	No	Ventricular septal defect; dextroposition of aorta; coarctation of aorta
Demonstrated aberrant left pulmonary artery	2½ yr.	Anomalous left pulmonary artery divided and re-anastomosed to the left of the trachea; postoperative angiocardiogram showed no filling of left pulmonary artery; stridor relieved	—	Yes	—
Demonstrated aberrant left pulmonary artery	2 yr.	Anomalous left pulmonary artery re-anastomosed medial to the trachea; postoperative cardiac arrest	2 yr.	Yes	No other cardiovascular anomalies
Demonstrated aberrant left pulmonary artery	—	None	—	Yes	—
—	2½ mo.	Left exploratory thoracotomy performed; anomalous left pulmonary artery not recognized	2½ mo.	No	None mentioned
	—	Repair of imperforate anus	4 da.	No	Repaired imperforate anus; harelip; cleft palate; persistent left superior vena ca into coronary sinus; atrioventricularis communis

TABI

CASE NO.	AUTHOR	SEX	AGE AT ONSET OF SYMPTOMS	DIAGNOSTIC TESTS		
				X-RAY CHEST	ESOPHAGRAM	BRONCHOSCOP
XII.	Sherman[10]	Male	Birth	Emphysema rt. lung; left mediastinal shift	—	—
XIII.	Present report	Female	Birth	Emphysema rt. lung; left mediastinal shift	Lateral indentation esophagus	Tracheo-bronchogram; no conti media into rt. main bronchus
XIV.	Present report	Female	Birth	Cardiomegaly	Normal	—
XV.	Present report	Male	1 mo.	Increased density rt. base	Anterior indentation esophagus	Tracheo-bronchogram; separati of trachea and esophagus

and aspirate, allowing simultaneous visualization of the esophagus and tracheobronchial tree. The aberrant pulmonary artery is well outlined by the resultant filling defects in the posterior trachea and anterior esophagus. It has been stated that the diagnostic identation of the esophagus is best seen in the lateral projection.[7] Our cases have been variable in this regard. In Case I, the esophagus appeared normal in the posteroanterior film while the lateral view showed deep anterior indentation; in Case III, the reverse was true. Ideally, posteroanterior, lateral, and oblique projections should be taken with radiopaque material in the trachea and esophagus. It should be emphasized that virtually the only other vessel which passes between the trachea and esophagus is an aberrant subclavian artery which, in 15 per cent of cases, lies between these two structures.[11] In this condition, however, the indentation of the esophagus is oblique in the posteroanterior projection and is seen at a higher level.

In cases of aberrant left pulmonary artery, the outstanding pathologic feature has been the uniformity of the anomaly. In each case it has consisted of an elongated main pulmonary artery segment with the left branch arising well in the right mediastinum and passing posteriorly between the trachea and esophagus to the left hilum. Either the trachea, the right main-stem bronchus or both may be obstructed as a result (see Fig. 1). The term "vascular sling"[9] has been proposed to differentiate this condition from the more common vascular ring anomalies.

NT'D

NGIOCARDIOGRAM	AGE AT OPERATION	OPERATION	AGE AT DEATH	DIAGNOSIS ANTE MORTEM	ADDITIONAL FINDINGS AT AUTOPSY
—	3 wk	Right middle and lower lobe lobectomies for obstructive emphysema, anomaly of pulmonary artery not recognized	6 mo	No	Bilateral obstructive emphysema, rt subclavian and rt and left common carotids arose from innominate artery
—	11 wk 14 wk	Right exploratory thoracotomy, anomaly of pulmonary artery not recognized Right exploratory thoracotomy, anomalous pulmonary artery thought to be a patent ductus and ligated	4 mo	No	Complete cartilaginous rings trachea, rt upper lobe artery from left pulmonary artery, persistent left superior vena cava entering coronary sinus, ostium secundum defect, eparterial right upper lobe bronchus
id not demonstrate anomalous pulmonary artery	—	None	4 yr, 11 mo	No	Tetralogy of Fallot with pulmonary atresia, ostium secundum defect, right aortic arch patent ductus arteriosus, persistent left superior vena cava into coronary sinus, single lobed left lung, rt upper lobe artery from left pulmonary artery
—	2 mo	Right exploratory thoracotomy, anomalous pulmonary artery thought to be anomalous aortic arch and ligated	2 mo	No	Ostium secundum defect, patent ductus arteriosus, cartilaginous rings, absence of gall bladder

Associated congenital anomalies are noted in Table I Of the 12 cases examined postmortem, complete tracheal cartilaginous rings were present in 3, while 4 patients had persistent left superior vena cava Four patients (Cases VI, XI, XIV, XV in Table I) had congenital cardiac anomalies, while 2 additional infants (Cases V, XII) had anomalies of the systemic arterial system

The embryologic origin of this defect is unknown The development of the left pulmonary artery from other than the usual channels of the primitive vascular plexus, which is the forerunner of the aortic arches, might lead to such an anomaly If this is true, the malformation dates from the fifth or sixth week of fetal life Many of the associated anomalies listed in Table I, including vena caval anomalies, cleft palate, and imperforate anus, probably date from the same stage of development

Surgical correction of this anomaly is achieved by dividing the aberrant pulmonary artery and re anastomosing it in front of the trachea This was done successfully in 2 of the 8 cases in which operation was performed (III and VII —Table I) Improvement in preoperative diagnosis and better understanding of the anomaly at the operating table should increase the success rate markedly

A right anterolateral approach gives the optimum exposure The azygos vein and pleura must be divided along the tracheoesophageal groove Failure to do this has resulted in failure to see the anomaly in several cases Fig 7 shows the vessel as seen from this approach The point of origin from the main pulmonary artery cannot be visualized in this limited dissection, consequently the vessel has been mistaken for part of an aortic ring anomaly. This should not be a source of confusion. To our knowledge, virtually the only other vessel which passes between the trachea and the esophagus is an aberrant subclavian artery[11]; this vessel does not encircle the trachea and is at a higher level.

In Case III, high pressure and the aspiration of arterial blood led to the division of the vessel with the presumptive diagnosis of double aortic arch. The explanation for this became apparent at postmortem examination. A patent ductus arteriosus emptied from the aorta into the main pulmonary artery just proximal to the origin of the aberrant left pulmonary artery. A large secundum atrial septal defect was also present, perhaps permitting additional right-to-left shunt.

The anastomosis must be done with great rapidity since the right lung is often compromised. Hypothermia might offer additional protection during performance of the anastomosis.

SUMMARY

Aberrant left pulmonary artery should be considered in the differential diagnosis of all infants with persistent stridor. In this condition, the left pulmonary artery arises in the right mediastinum and passes posteriorly between the trachea and esophagus to the left lung, resulting in obstruction of the trachea or right main-stem bronchus.

Fifteen cases of this anomaly are summarized. Diagnosis can be readily established by combined tracheo-esophagram. Surgical correction is discussed.

The authors wish to thank Dr. John Caffey and Dr. Sidney Blumenthal for their advice and encouragement in the preparation of this manuscript.

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A COMPARATIVE STUDY OF HEPARIN NEUTRALIZATION AND THE DANGER OF BLOOD CLOTTING ABNORMALITIES WITH PROTAMINE AND POLYBRENE

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The rapid increase in use of extracorporeal circulation has emphasized the need for optimum control of anticoagulation and coagulation of blood. Although protamine sulfate will completely neutralize heparin, it has a specific anticoagulant action of its own and has been incriminated as a possible cause of clotting abnormalities after perfusion[1, 4]; a certain incidence of undesirable systemic reactions has also been recorded. A drug with equal heparin-neutralizing properties, but which could be used with greater safety, would be highly desirable. Polybrene,† a polymeric quaternary ammonium salt, has recently been proposed as such an agent and studies have been performed indicating that it will produce satisfactory neutralization of heparin[5, 7]; however, data on its in vivo anticoagulant activity have not been presented, and the quantitative aspects of heparin neutralization in comparison with protamine have not been well defined.

In a series of animal experiments, Polybrene and protamine sulfate were compared with respect to effectiveness of heparin neutralization and neutralizing dosage levels, and quantitative studies were performed of in vivo anticoagulant effect of each drug at dosage levels within the range commonly employed clinically.

METHODS

Adult mongrel dogs were lightly anesthetized with intravenous Pentothal and plastic cannulae were introduced through the femoral veins into the inferior vena cava for blood sampling. Before collection of each sample the cannulae were flushed by preliminary withdrawal of blood.

Heparin neutralization was estimated by titrations[1] using protamine or Polybrene, respectively, and the clotting time was measured simultaneously

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*Markle Scholar in Medical Science.

†Polybrene (hexamethrine bromide) supplied by Abbott Laboratories, Chicago, Ill.

with each titration by a three-tube Lee-White technique. The titration was used to indicate the relative degree of neutralization of heparin or excess of the neutralizing agent and the coagulation time was used as a more precise quantitative measure of the clotting time.

DESIGN OF EXPERIMENTS

Adult mongrel dogs in pairs of similar weight were selected at random. Experiments were performed using Polybrene in one dog of each pair and protamine* in the other, with each of the stages of the experiments carried out at identical times. This technique seemed satisfactory from the standpoint of providing comparative information on the relative effect of the two drugs at risk.

Studies were performed in 20 animals with protamine and in a concomitant group of 20 animals with Polybrene. In each animal, a control titration was performed and clotting time determined and then heparin,† 2.5 mg. per kilogram, was administered intravenously. Fifteen minutes after the administration of heparin, the titration was repeated and coagulation time determined, followed immediately by the intravenous administration of a predetermined amount of neutralizing agent. At subsequent 15-minute intervals, repeat titrations were performed and coagulation times determined and additional amounts of the neutralizing agents were given until a total dose equal to 200 per cent of the original heparin dose by weight was reached. In each pair of experiments, identical amounts of protamine and Polybrene were given at each stage, calculated on a body-weight basis.

RESULTS

The qualitative results in each group are given in Tables I and II. Significant inhibition of clotting by the heparin-neutralizing agent was considered to be present only in those animals in which titration indicated an excess and the clotting time was increased by 5 minutes or more above either the control level or the lowest post-neutralization level. For this evaluation a clotting time within 5 minutes of control levels was considered as demonstrating satisfactory neutralization. By this standard, 12 of 20 dogs in which heparin was neutralized by protamine showed inhibition of clotting due to protamine. Inhibition occurred chiefly at dosage levels of 150 to 200 per cent of the original heparin dose by weight. In the Polybrene-treated dogs, inhibition of clotting occurred in 11 of 20 dogs, with the majority of instances of inhibition occurring at the 150 per cent and 200 per cent dosage levels. There was no significant difference between protamine and Polybrene in the incidence of inhibition of coagulation.

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*Protamine sulfate injection, 1 per cent, was used in all experiments. (Supplied by Eli Lilly Co., Indianapolis, Ind.)

†Heparin sodium, 1,000 units per cubic centimeter (10 mg.), was used in all experiments. (Supplied by Abbott Laboratories, Chicago, Ill.)

TABLE I*

EXPERIMENT NUMBER	POLYBRENE DOSAGE IN PER CENT OF HEPARIN GIVEN						
	50%	75%	90%	100%	125%	150%	200%
1	0			0		+	+
2	—			0		0	0
3		0				0	0
4		0				0	0
5		0				+	+
6			+			+	+
7			0			0	0
8			0			+	+
9				0		0	0
10				0		0	0
11				0		+	+
12				0		0	+
13				+		+	+
14				0		0	+
15					0		0
16					0		+
17					0		0
18						+	+
19						+	+
20						0	0
Totals							
–	1						
0	1	3	2	7	3	9	9
+			1	1		8	11

*(–) indicates heparin excess as determined by titration (0) indicates complete neutralization of heparin with clotting time essentially normal (+) indicates protamine excess with clotting time prolonged more than 5 minutes above control or lowest post-neutralization time

TABLE II*

EXPERIMENT NUMBER	PROTAMINE DOSAGE IN PER CENT OF HEPARIN GIVEN						
	50%	75%	90%	100%	125%	150%	200%
1	—			+		+	+
2	0					0	0
3		0		+		+	+
4		0				0	+
5		0				0	0
6			0			+	+
7			0			+	+
8			0			0	0
9				0		0	0
10				0		+	+
11				0		0	0
12				0		+	+
13				0		+	+
14				0		+	+
15					0		+
16					0		0
17					0		0
18						0	+
19						0	+
20						0	0
Totals							
–	1						
0	1	3	3	6	3	9	8
+				2		8	12

*(–) indicates heparin excess as determined by titration (0) indicates complete neutralization of heparin with clotting time essentially normal (+) indicates protamine excess with clotting time or lowest post-neutralization time

The mean increase in clotting time above optimum levels, as determined by the three-tube coagulation time, was 5.5 minutes in the group treated with protamine and 7.7 minutes in the group receiving Polybrene (Table III). In each case this is a significant increase in coagulation time as compared to control levels ($0.01 > P > 0.001$). However, the difference between protamine and Polybrene is not significant ($0.40 > P > 0.30$). Protamine did not produce prolongation of clotting times of the magnitude seen in several experiments with Polybrene (Experiments 6, 13, 18).

TABLE III. INCREASE IN CLOTTING TIME ABOVE CONTROL LEVELS (IN MINUTES)*

EXPERIMENT NUMBER	PROTAMINE	POLYBRENE
1	+10	+ 7.5
2	0	0
3	+16	0
4	+ 6.5	0
5	0	+ 8
6	+18	+29
7	+ 6.5	0
8	0	+ 8.5
9	0	0
10	+ 5.5	0
11	0	+ 7
12	+15	+13.5
13	+ 7.5	+26.5
14	+ 5.0	+ 7.0
15	+ 6.5	0.0
16	0.0	+14.0
17	0.0	0.0
18	+ 5.0	+19.0
19	+10.0	+15.0
20	0.0	0.0
Mean	5.5	7.7
S. D.	7.7	11.5
S. D. Mean	1.73	2.6

*In each instance the maximum increase in clotting time above control levels is recorded. This increase usually, but not always, occurred at the maximum level of protamine administration.

With each drug, dosages of 75 per cent or more by weight of the original heparin doses consistently produced complete neutralization of the heparin and restored the clotting time to normal.

DISCUSSION

A close examination of data in published studies on the neutralization of heparin by protamine or Polybrene indicates that it is not uncommon for the clotting time to fail to return entirely to normal levels after apparently adequate neutralization. Abnormal coagulation of the blood has also been noted frequently after neutralization of heparin following total body perfusion with an artificial pump-oxygenator, even though titration tests eliminate inadequate heparin neutralization as a cause for the observed abnormality in clotting.

Although the potential danger of protamine as a specific anticoagulant has been mentioned as a possible cause of this abnormality,[1, 4] quantitative in vivo studies of this potential hazard have not been presented. Similarly, although Polybrene has a known anticoagulant effect in vitro,[6] there has been no quantitative data from in vivo studies. Previous experimental studies[1] on the activity of heparin and aspects of protamine neutralization have demonstrated that it is not uncommon to have protamine inhibition of clotting after administration of doses comparable to those used clinically. Although the resultant defect in coagulation is ordinarily small, it may be great enough to produce abnormal bleeding.

The present studies and others[1, 2, 3] suggest that the commonly used neutralizing dosages of 100 per cent to 200 per cent by weight of the heparin given may be unnecessarily large and, in fact, hazardous. Further, in these studies the initial neutralizing dose was given only 15 minutes after administration of heparin; with the passage of time there is a rapid decrease in the active heparin level, so that progressively smaller amounts of neutralizing drugs are required to restore normal blood clotting.[1]

In our initial experimental experience with Polybrene, it appeared that a more normal coagulation time was obtained than with protamine. This observation seems to be explained by the smaller amounts of Polybrene which we used, 0.7 to 1.0 times the amount of heparin given. Since the heparin-neutralizing properties of the two drugs are approximately equal by weight, use of a larger dose with one or the other will tend to produce a proportionately greater incidence of inhibition of clotting due to excess. The data obtained in these comparative experiments do not indicate any significant difference between Polybrene and protamine, either in effectiveness of heparin neutralization or in tendency to produce inhibition of blood clotting with excessive doses.

Although these data may not be directly applicable to the post-perfusion state, they suggest that a more cautious use of these drugs in neutralizing heparin after extracorporeal circulation may lessen the incidence of unexplained abnormalities in bleeding and clotting.

SUMMARY

1. A comparative experimental study of in vivo heparin neutralization and production of inhibition of blood clotting by protamine and Polybrene was carried out in dogs.

2. Dosages of 75 per cent or more by weight of the original heparin dose were consistently sufficient to produce complete heparin neutralization with either protamine or Polybrene.

3. Both protamine and Polybrene produced significant elevation of coagulation time above control levels in over 50 per cent of these experiments. The abnormalities of clotting occurred chiefly at dosages of 150 to 200 per cent of the heparin dose by weight, well within the range in common clinical use for heparin neutralization. This dosage ratio is unnecessarily large for optimal neutralization.

4. The increase in coagulation time produced by these drugs in the dosages used were small compared to that produced by heparin. Nevertheless, it may be sufficient to cause significant bleeding.

5. No definite superiority of either drug was evident in the parameters tested.

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THE EFFECT OF 2 PER CENT CARBON DIOXIDE ON pH AND pCO_2 DURING EXTRACORPOREAL CIRCULATION

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CARBON DIOXIDE is routinely added to artificial oxygenators during extracorporeal perfusion, and yet, there is no evidence to indicate that this is necessary Bjork[1] observed an uncompensated carbon dioxide deficit with an increase in pH when the brain alone was perfused with 100 per cent oxygen in the oxygenator Stokes and Gibbon[2] showed similar changes during recirculation prior to perfusion However, they also observed that when the animal's metabolic carbon dioxide had to be removed, the use of 100 per cent oxygen proved necessary to wash out this carbon dioxide and keep the pH within a normal physiologic range Mendelsohn and his associates[3] warned against excessive "carbon dioxide wash out" during perfusion with 100 per cent oxygen

We, on the other hand, observed in the laboratory that prolonged perfusion utilizing 100 per cent oxygen in the oxygenator did not result in this so called 'carbon dioxide wash out " Therefore, we elected to omit carbon dioxide in a series of patients and compared the results from this group with the results obtained in patients in whom 2 per cent carbon dioxide was added to the oxygenator

METHODS

Data were obtained from 56 patients undergoing 57 separate perfusions In 35 perfusions, 100 per cent oxygen was passed through the oxygenator, in the remaining 22 cases, a mixture of 98 per cent oxygen and 2 per cent carbon dioxide was used at flow rates of 8 to 10 L per minute All patients were perfused with a rotating disc oxygenator[4] Duration of total cardiopulmonary bypass ranged from 9 to 92 minutes Flow rates varied between 50 c c per kilogram per minute (adults) and 140 c c per kilogram per minute (small children) and averaged 80 c c per kilogram per minute The ages of the patients varied from 2 5 to 61 years and their weight from 12 2 to 80 05 kilograms

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The blood was initially oxygenated with room air by slowly revolving the discs through the priming volume in the oxygenator. No gases were passed through the oxygenator until just prior to the start of perfusion. In this way, low initial carbon dioxide tension in the extracorporeal circuit was avoided.

Arterial and venous blood samples were obtained from the extracorporeal system at the start and finish of the period of total cardiopulmonary bypass. In addition, pre-perfusion samples were obtained from 18 patients. Samples were kept under oil in a buffered fluoride solution at 4° C. until analyzed within a few hours. Oxygen and total carbon dioxide were measured after Van Slyke and Neill.[5] A Cambridge Research Model pH meter was used to measure blood pH. All values were corrected to 37° C. Blood pCO_2 was calculated from pH and total carbon dioxide according to the nomogram of Van Slyke and Sendroy.[6] The electroencephalogram and electrocardiogram were monitored continuously during perfusion.

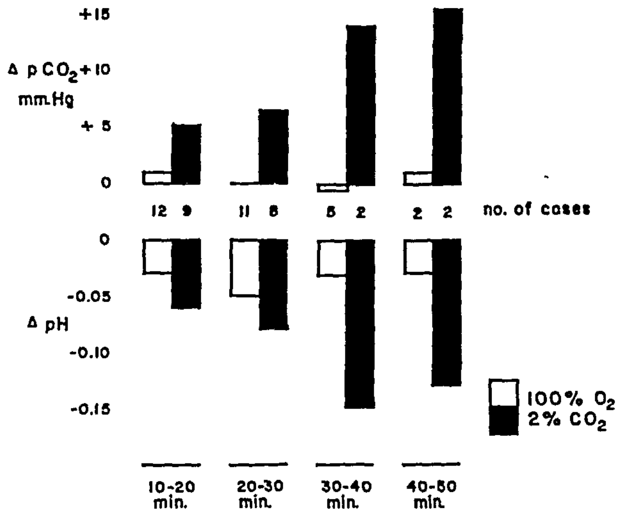

Fig. 1.—Change in pH and pCO_2 as related to perfusion time.

RESULTS

Data relating to perfusion are summarized in Table I. The average fall in arterial pH during perfusion in the cases in which 100 per cent oxygen was employed was from 7.39 to 7.35 while pCO_2 increased slightly from 23.8 to 24.1 mm. Hg. In the second group in which 2 per cent carbon dioxide was added during perfusion, the arterial pH fell from 7.32 to 7.23 at the same time that the pCO_2 rose from 31.3 to 38.6 mm. Hg. The higher initial value of pCO_2 observed in this second group is explained by the fact that extra carbon dioxide had been flowing into the oxygenator for several minutes during the period of partial perfusion and before the blood samples were obtained. There was a significant difference in the changes in these two groups.

The effect of duration of perfusion is shown in Fig. 1. When no carbon dioxide was added, lengthening perfusion did not result in a fall in pCO_2 or in a progressive fall in pH. In contrast, when carbon dioxide was added, increasing perfusion time up to 50 minutes resulted in an increase in pCO_2 and a decrease in pH. In 3 cases, not included in this figure, in which perfusion lasted over an hour and 100 per cent oxygen was used, there was no significant change in either pH or pCO$_2$.

The relation between pH and pCO$_2$ in the final arterial sample is shown in Fig. 2. In 30 of the 35 perfusions in which no carbon dioxide was added, the pH was greater than 7.30 and the pCO$_2$ was less than 30 mm. Hg in all but one. Four patients in this group showed a final pCO$_2$ of less than 20 mm. Hg. All 4 patients, however, started with a low pCO$_2$ due to hyperventilation by the anesthesiologist prior to perfusion and all 4 survived without complications. In all 35 cases, the electroencephalogram remained normal. In 19 of the 22 perfusions in which 2 per cent carbon dioxide was added during perfusion, the pH fell below 7.30. In all 22 cases the pCO$_2$ was greater than 30 mm. Hg.

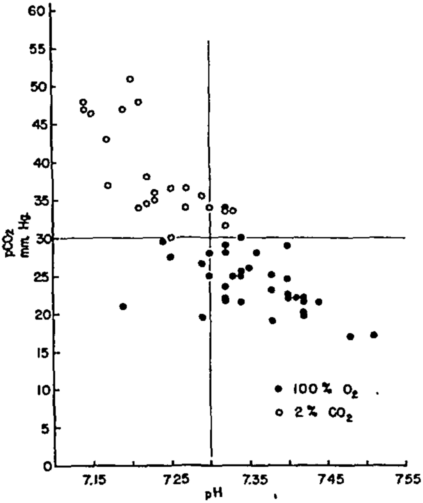

Fig. 2.—Relation between arterial pH and pCO$_2$ at the finish of perfusion.

In patients in whom a respiratory alkalosis was created by hyperventilation before perfusion, the pH tended to return to normal values, but the pCO$_2$ remained low if 100 per cent oxygen was used. If carbon dioxide was added, the pH fell as the carbon dioxide rose.

TABLE I. AVERAGE CHANGE IN pH AND pCO$_2$ DURING EXTRACORPOREAL CIRCULATION

		START	FINISH	CHANGE*	SIGNIFICANCE
pH	100% O$_2$	7.39	7.35	−0.04 ± 0.04	$p < 0.003$
	2% CO$_2$	7.32	7.23	−0.09 ± 0.06	
pCO$_2$	100% O$_2$	23.8	24.1	+0.3 ± 4.2	$p < 0.001$
	2% CO$_2$	31.8	38.6	+7.3 ± 5.3	

*Mean ± standard deviation.

DISCUSSION

Using the same oxygenator as Mendelsohn and his co-workers,[3] we have not been able to confirm their observation that "if carbon dioxide is not added to the oxygenator, a marked respiratory alkalosis occurs, with carbon dioxide 'washout'."[7] To the contrary, our observations in patients show that carbon dioxide tension in arterial blood is maintained at nearly constant levels when carbon dioxide is omitted. DeWall,[8] Helmsworth[9] and their co-workers have also observed minimal change in pCO_2 during perfusion. The slight fall in pH in the patients in whom 100 per cent oxygen was used is consistent with the known development of metabolic acidosis that occurs during perfusion, irrespective of the type of oxygenator employed.[3, 8, 10, 11, 12] That this fall in pH was minimal in these cases is probably related to the high perfusion rates used in this series. Addition of carbon dioxide during perfusion does not compensate for this metabolic acidosis but, by superimposing a respiratory acidosis depresses pH even further.

The constancy of the arterial pCO_2 when 100 per cent oxygen is used is difficult to explain. Mechanical factors of the oxygenator can be excluded since no change in pCO_2 was noted whether perfusion was maintained at 1,200 or 2,600 c.c. per minute or for 9 or 60 minutes with the same sized oxygenator at the same oxygen flow rate. The possibility arises, therefore, that there is an inrinsic mechanism in the blood buffer systems (hemoglobin, plasma proteins, phosphate, etc.) that maintains carbon dioxide tension under the conditions of total body perfusion.

The low pCO_2 observed in some of our patients and also in those reported by Mendelsohn[3] was due to hyperventilation by the anesthesiologist prior to perfusion. Carbon dioxide tension can be maintained by controlling repiration, avoiding hyperventilation by the anesthesiologist, and by passing oxygen through the artificial lung only during the period of perfusion. It is of interest that even in those patients in whom pCO_2 was less than 20 mm. Hg, no electroencephalographic abnormalities were observed and all these patients survived. The clinical observations herein reported support experimental evidence that cerebral circulation during perfusion is not significantly affected by the pCO_2 level.[13, 14]

CONCLUSIONS

This clinical study shows that the use of 100 per cent oxygen in an artificial oxygenator does not result in pCO_2 washout. In fact, the pCO_2 remains constant under these conditions and minimal pH changes occur.

On the other hand, addition of carbon dioxide results in a rise in pCO_2 and thereby adds a respiratory acidosis to the metabolic acidosis occurring with perfusion. It is, therefore, concluded that it is not necessary and, in fact, may be detrimental to add carbon dioxide to artificial oxgenators during extracorporeal circulation.

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SIMPLIFIED FLOW DETERMINATION, VOLUME CONTROL, AND BLOOD REPLACEMENT IN THE ROTATING DISC OXYGENATOR

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MECHANICAL DISADVANTAGES in operation of the Kay-Cross oxygenator[1] in combination with the De Bakey roller pumps have been observed by us in clinical and laboratory perfusions. These deficiences include:

1. Rapid changes in oxygenator reservoir fluid level which may be associated with (a) going on bypass, (b) going off bypass, (c) initial removal of blood from within a large heart and the reverse situation when cardiotomy is closed, (d) blood loss in operative field, (e) caval cannula occlusion, and (f) use of a sopressor.
2. Interference with oxygenator efficiency when fluid level changes within oxygenator. (This can be disastrous if volume change is sudden and large, a situation not infrequent at high flow rates in adults.)
3. Difficulty in rapidly removing or adding blood to oxygenator reservoir in event of fluid fluctuations.
4. Difficulty in accurately determining output of partially occlusive roller pumps.
5. Inability to determine accurately pre-perfusion and post-perfusion volume in oxygenator reservoir because of large cross-sectional area.
6. Occasional formation of small surface bubbles in oxygenator reservoir.

Minor modifications designed by one of us (R.S.C.) have virtually eliminated these problems in our artificial heart-lung: (1) gravity drainage of caval blood to a vertical receiving reservoir of large capacity (2,650 c.c.) but of small cross-sectional area (1 cm. fluctuation = 50 c.c. or with central obturator 1 cm. fluctuation = 25 c.c.) (Fig. 1), and (2) addition of an overflow tap at the desired blood level in the arterial end-plate (Fig. 2).

With these adjuncts a drainage line between the overflow tap and the receiving reservoir bleeds back excess blood, and constant oxygenator reservoir volume is automatically obtained by simply maintaining the output of the venous pump slightly greater than that of the arterial pump (Fig. 3). Prior

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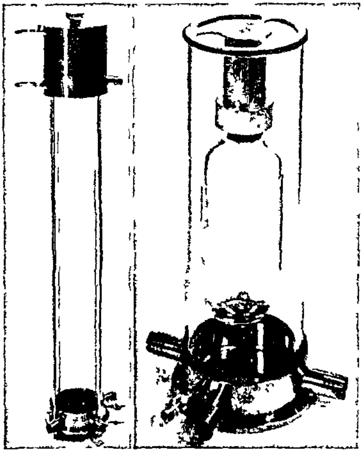

Fig 1 —*A*, Gravity drainage receiving reservoir Pyrex glass cylinder is 51 cm long with an internal diameter of 8 cm Taps on base plate are used for (1) caval cannula drainage, (2) venous pump line (3) overflow line and (4) left atrial drainage Intracardiac blood returned through tap on reservoir head is directed to flow down side of reservoir

B, Central obturator increases accuracy if desired in small patients

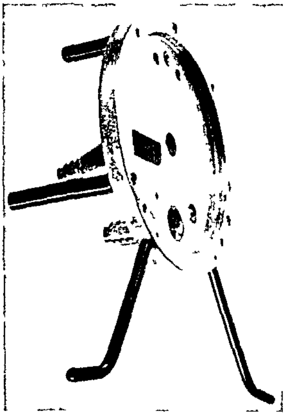

Fig 2 —Prototype model arterial end plate with rectangular over-flow tap 4 by 1 5 cm in size Lower edge of tap is at height of desired blood level, and inner border is beveled slightly to avoid hold up due to surface tension

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to bypass, blood is cycled allowing one to determine variations of the fluid level in the receiving reservoir due to build up on the upturn side of the discs and at the venous end of the oxygenator reservoir These volumes are usually small but may be considered when regulating extracorporeal volume during bypass Variation in extracorporeal volume is then reflected in the receiving reservoir where the accuracy of measurement equals that of a graduated cylinder in which 1 cm equals 50 c c volume In children, the central obturator may be added, a shorter, smaller volume reservoir utilized, and reading accuracy increased with a centimeter fluctuation equaling 25 c c (Fig 1, *B*) An inexpensive pulley system permits control of receiving reservoir height with variation of amount of negative venous line pressure as desired

Immediate automatic replacement of operative blood loss up to 2,000 c c occurs since this blood is carried in the receiving reservoir once bypass is established Additional blood can be rapidly added from the donor reservoir

Since input and output resistance is known when pumping from a receiving reservoir to an oxygenator reservoir where volume is constant, the partially occlusive venous pump properly calibrated prior to bypass becomes a reliable flow meter Fig 4 shows the linear relationship between pump speed and pump output under these circumstances Measurement has shown the volume passing through the overflow tube during bypass to be 60 c c of blood per minute when a small trickle is maintained The actual volume can be determined by clamping the overflow line and measuring the time volume relationship Naturally, the overflow volume is considered when calculating the arterial pump output on the basis of the venous pump revolutions per minute

An unexpected advantage is that the overflow tap system efficiently removes the bubbles which form on the surface of the fluid level of the oxygenator where the discs enter the blood *

Use of this system in bypass procedures has been uniformly satisfactory An extremely accurate blood balance, avoidance of undesirable fluid fluctuations within the oxygenator reservoir, and immediate replacement of blood loss have materially reduced sources of human error in the operation of this apparatus The set up avoids the undesirable rigidity of electrical regulating systems and permits control utilizing the central venous pressure parameter

SUMMARY

1 Mechanical operation of the Kay Cross oxygenator with partially occlusive De Bakey roller pumps has been simplified by (a) gravity drainage to a vertical receiving reservoir of small diameter but large capacity, and (b) addition of an overflow tap to the arterial end plate of the oxygenator reservoir

2 These modifications have resulted in (a) accurate extracorporeal volume determination, (b) automatic volume control within the oxygenator reservoir, (c) immediate blood replacement of up to 2,000 c c in the event of sudden blood loss, (d) reliable flow determination utilizing the partially occlusive venous

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*Direction of disc rotation may require reversal in certain commercially available systems since it is desirable to have the lower more stable level facing the pump operator pump, (e) removal of surface bubbles by way of the overflow tap, (f) transfer of fluid fluctuations to the noncritical receiving reservoir, (g) avoidance of the undesirable rigidity of electrical regulating systems, and (h) ready control of venous line negative pressure.

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A SYSTEM FOR HYPOTHERMIC PERFUSION

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THE COMBINATION of hypothermia and total body perfusion has many desirable features.[1-7] Rapid changes in the temperature of blood are accomplished by heat exchangers interposed in a heart-lung machine circuit.[6, 7] A new simple technique of internal cooling and warming is described, its safety features discussed, and its advantages stressed.

DESCRIPTION OF APPARATUS FOR INTERNAL COOLING AND WARMING OF BLOOD

Internal cooling is accomplished by pumping water at 4° C. countercurrently through a 325 cm. long, 22-gauge, stainless steel spiral inserted in the Mayon helix of a DeWall-Lillehei heart-lung machine (Fig. 1). The latter is not immersed in the customary water jar, as the heat exchange across the Mayon tubing is minimal.[8] This system is inexpensive, plain in design, easily assembled, and simply cleaned. The blood and water circuits are completely separated and the heat transfer coefficient compares favorably with the Brown exchanger.[7] The priming volume of the helix is reduced without altering the efficiency of the system as a bubble separator.

The internal warming device, in addition, consists of stainless steel tubes bent in the shape of hairpins and placed in the venous reservoir (Fig. 2). Fig. 3 is a diagram of the cooling and warming system used with a DeWall-Lillehei bubble oxygenator for total body perfusion.

TECHNIQUE OF HYPOTHERMIC PERFUSION FOR OPEN HEART SURGERY

External cooling is carried out during the preparatory phase of surgery, and internal cooling is started when cannulation of both venae cavae and femoral artery is completed. The perfusion rate is preset at 20 c.c. per kilogram of body weight and heparin, 1.5 mg. per kilogram of body weight, is given intravenously. At an intraesophageal temperature of 30° C., the aorta is clamped distal to the coronary ostia for periods of 15 to 25 minutes at a time during the repair of the intracardiac defects. Warming is started a few minutes before the anticipated termination of the corrective procedures and the temperature is usually about 36° C. by the time the chest is closed. Polybrene† is usd to counteract heparin.

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†Supplied by Abbott Laboratories, Chicago, Ill.

EXPERIMENTAL DATA

Extensive investigation preceded the experimental and clinical adoption of this technique and will be reported separately. . Consistent survival was obtained in a consecutive series of 8 dogs following 30 minutes of aortic occlusion at 20° C. and right ventriculotomy.

CLINICAL DATA

The clinical data on the first 7 consecutive patients who underwent hypothermic perfusion by the technique described are summarized in Tables I-III.

TABLE I. CLINICAL DATA ON 7 PATIENTS WHO UNDERWENT HYPOTHERMIC PERFUSION

PATIENT	AGE (YR.)	WEIGHT (KG.)	DIAGNOSIS	FLOW RATE (C.C./KG. BW/MIN.)	TOTAL BLOOD USED
1	31	70	I.A.D.*	20	3,500
2	43	50	I.A.D.	20	3,000
3	4	16.3	T.O.F.†	20	2,500
4	14	35	T.O.F.	20	7,000 (Blood loss through a patent ductus arteriosus)
5	4	14.5	Pulmonary valvular and infundibular stenoses	20	2,000
6	11	43	I.A.D.; explored for possible pulmonary stenosis	20	2,000
7	35	43	Mitral commissurotomy	20	2,750

*Interauricular defect.
†Tetralogy of Fallot.

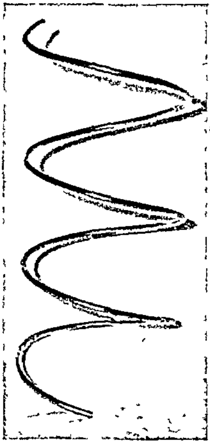
TABLE II. HYPOTHERMIC PERFUSION DATA ON 7 CONSECUTIVE PATIENTS

PATIENT	TOTAL PERFUSION TIME (MIN.)	DURATION OF AORTIC OCCLUSION (MIN.)*	DURATION OF CARDIAC REPAIR (MIN.)	TEMPERATURE RANGE DURING AORTIC OCCLUSION
1	38	15†	22	27° C.-30° C.
2	41	13†	20	29° C.-30° C.
3	69	22‡	56	26° C.-30° C.
4	121	66 (20, 23, 7 and 16)‡	110	27° C.-30° C.
5	124	0‡	33 and 30	23.5° C.-31° C.§
6	75	24 (18, 6)‡	41	27° C.-30° C.
7	38	18‡	28	26° C.-30° C.

*Figures between parentheses indicate, in minutes, periods of successive aortic occlusion.
†Ventricles continued to beat regularly.
‡Ventricular fibrillation that responded immediately and reverted to regular rhythm upon allowing coronary flow and applying a single shock of 110 to 135 volts for 0.1 second.
§During cardiac repair.

DISCUSSION

The advantages of this technique for hypothermic perfusion and intracardiac surgery are multiple. The system is clean, inexpensive, locally accessible, and dependable. It decreases the priming volume and preserves all the features of the DeWall helix. The low flows permitted at these reduced temperatures slow down the "tempo" and allow for lengthy perfusions and rather prolonged periods of repeated aortic occlusions. This offers virtually an empty heart and abolishes the fear of air embolism. The ventricles usually



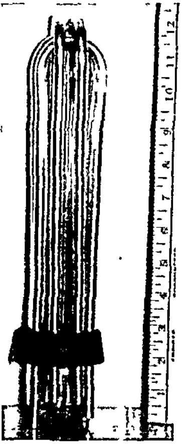


Fig. 1 Fig. 2

Fig 1.—Stainless steel inner helix, a component of the heat exchanger

Fig 2—Stainless steel "hairpins" inserted in the venous reservoir—the second component of the heat exchanger.

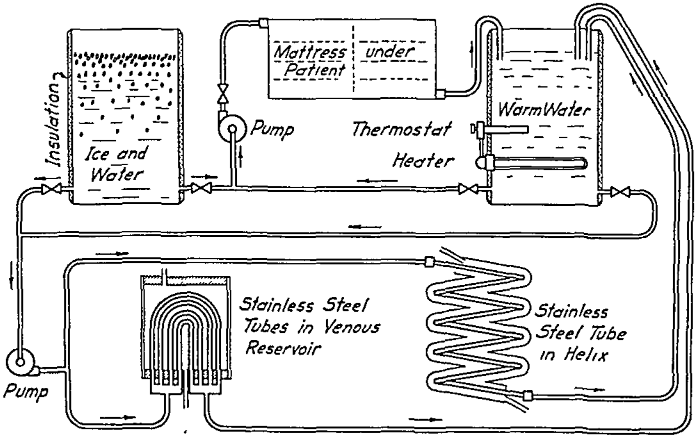


Fig 3—A diagram of the entire heat exchange system

TABLE III. SOME PHYSIOLOGIC DATA ON 7 CONSECUTIVE PATIENTS WHO UNDERWENT HYPOTHERMIC PERFUSION

PATIENT	EEG DURING PERFUSION*	POSTOPERATIVE ECG	RANGE OF PERIPHERAL OXYGEN SATURATION DURING PERFUSION* (PER CENT)	RESPONSE FROM ANESTHETIC	FINAL OUTCOME
1	Adequate	No ischemia or infarction	85-98	Immediate; no pathologic or neurologic signs	Living and well
2	Adequate	No ischemia or infarction	90-97	Immediate; no pathologic or neurologic signs	Living and well
3	Adequate	No ischemia or infarction	90-98	Immediate; no pathologic or neurologic signs	Died on 2nd p.o. day after doing well Autopsy: disruption of I.V. repair
4	Flattening of EEG at beginning due to PDA and then adequate	No ischemia or infarction	85-96	Immediate; no pathologic or neurologic signs	Living and well
5	Adequate	No ischemia or infarction	90-96	Immediate; no pathologic or neurologic signs	Living and well
6	Adequate	No ischemia or infarction	90-96	Immediate; no pathologic or neurologic signs	Living and well
7	Adequate	No ischemia or infarction	—	Immediate; no pathologic or neurologic signs	Living and well

*Traced with Electronics for Medicine Research recorder.

fibrillate after about 15 minutes of anoxia but revert promptly to a regular rhythm upon release of the aorta and applying a single shock of 110 to 135 volts for 0 1 second Electrocardiograms revealed no signs of ischemia or infarction at the end of the perfusion or postoperatively Electroencephalograms remained essentially unchanged during the cardiopulmonary bypass The peripheral oxygen saturations as measured with an earpiece usually read above 90 per cent (see Table III) All patients did well except a patient (No 3) who died in the second postoperative day after apparently doing well Autopsy revealed a disruption of the repair of the interventricular defect

SUMMARY

A simple system for open heart surgery, consisting of hypothermic perfusion and aortic occlusion, is described

Thanks are due for the unselfish help of Sister Mary Alvera, Modine Pierce, and John Montroy, Jr

ADDENDUM

Since the submission of this paper, our system was changed to consist of only the inner stainless steel helix for heat exchange Both the mattress and the hairpin shaped stainless steel tubes have been eliminated Up to this date (Feb 11, 1960), 38 patients had various heart defects repaired with this technique with 30 consecutive survivals Patient 2 died 4 months after surgery and autopsy revealed an intact interatrial repair and acute pancreatitis Patient 3 died on the second postoperative day and autopsy revealed disruption of the interventricular repair Patient 8 died on the third postoperative day and autopsy disclosed intact cardiac repair and severe bilateral pneumonia Both patients had tetralogy of Fallot

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OPEN VERSUS CLOSED LEFT ATRIAL DRAINAGE DURING CROSS-CLAMPING OF THE THORACIC AORTA

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THE HAZARDS of cross-clamping the aortic arch distal to the carotid arteries fall into two categories. First is proximal hypertension, which may cause cerebral hemorrhage, cardiac dilatation with ventricular fibrillation, and occasionally pulmonary edema. The second is inadequate blood flow distal to the clamp, which may result in spinal cord damage or ischemic renal insufficiency. The treatment of aneurysms of the distal aortic arch necessitates cross-clamping of the aorta. The method currently employed to obviate these dangers is the pumping of blood from the left atrium to the femoral artery via a closed system.[1] This procedure has not been entirely satisfactory, however, for De Bakey recently stated that 2 of 36 patients so treated have suffered ischemic spinal cord damage following cross-clamping of the descending thoracic aorta, in spite of left atrial to femoral artery bypass.[1] A recent clinical case at the Oklahoma City Veterans Administration Hospital, in which closed left atrial drainage was employed, revealed inadequate proximal decompression with a systolic pressure greater than 250 mm. Hg and transient pulmonary edema in spite of pump flow settings which were increased to greater than 3 L. per minute. This patient developed hypertensive encephalopathy postoperatively, but eventually made a complete recovery. The experience prompted us to study closed left atrial drainage experimentally, and compare it to open, or reservoir, drainage.

MATERIALS AND METHODS

Mongrel dogs, weighing 25 to 35 kilograms, were anesthetized with intravenous Nembutal. Ventilation was maintained by a mechanical respirator. Through a left thoracotomy, a 30 Fr. catheter was inserted into the left atrium. Blood could be drained by either open or closed methods by means of plastic tubing and pumped into the femoral artery via a totally occlusive Sigmamotor finger pump which had been previously calibrated. This pump, when totally occlusive, delivers a constant flow against the pressures encountered in this experiment.[2] A side-arm was provided to measure the actual flows delivered

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(Fig. 1). Pressures were measured in the carotid, femoral, and pulmonary arteries, pulmonary veins, and left atrium by means of polyethylene catheters, Statham strain gauges, and a Sanborn direct-writing oscillograph. Forty-one paired flow measurements of open and closed left atrial drainage were made on 13 dogs, utilizing flow settings between 500 and 2,600 c.c. per minute.

RESULTS

In 40 of these 41 flow measurements, closed drainage delivered less than the calibrated flow (Fig. 2). The single instance in which the flow from closed drainage equaled that of open drainage occurred in a dog which was hypervolemic and at a flow setting of only 500 c.c. per minute.

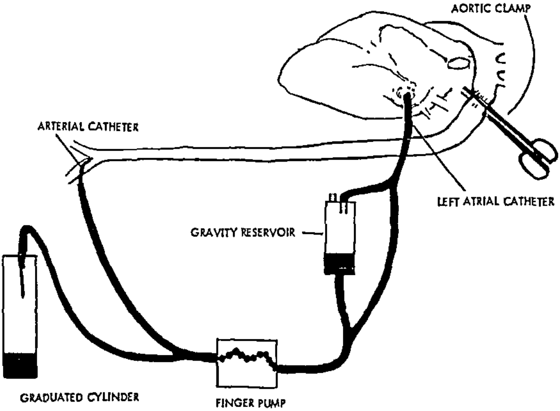

Fig. 1.—Diagram of method for study of open and closed left atrial drainage during left atrial to femoral artery bypass.

The dog's blood volume is an important determinant of the amount of blood drained from the left atrium (Fig. 3). With the pump set at 2,580 c.c. per minute during aortic arch cross-clamping, this volume of blood drained openly from the left atrium into a reservoir and was pumped into the femoral artery. This was the actual volume delivered, for the blood level in the reservoir remained constant. When the system was converted to closed atrial drainage, flow dropped to 525 c.c. per minute. With the measured withdrawal of serial volumes of blood, the amount of flow diminished progressively. After the loss of approximately one sixth of the dog's blood volume, flow had diminished to 195 c.c. per minute at a pump setting of 2,580 c.c. per minute. All 13 dogs showed this progressive decrease in closed bypass flow volumes with serial blood withdrawals; also, with flow settings as low as 500 c.c., progressive decrease in blood volume was accompanied by decrease in flow. Thus, at a setting of 500 c.c. per minute, closed bypass flow as low as 35 c.c. per minute was recorded in a hypovolemic dog. This relationship is of extreme practical importance, for many surgeons, fearing proximal hypertension during aortic cross-clamping, prefer hypovolemia at this time.

Pressure measurements during thoracic aorta cross-clamping alone are represented in Fig. 4. The pulmonary venous pressure, represented by the mean pulmonary artery wedge tracing, was originally 5 mm. Hg and after aortic cross-clamping increased to 17 mm. Hg. After release of the clamp it rapidly fell to its original level. The arterial side of the pulmonary capillary bed, represented by the pulmonary venous wedge pressure, remained constant at a mean of 27 mm. Hg during this 20-second period of aorta cross-clamping.

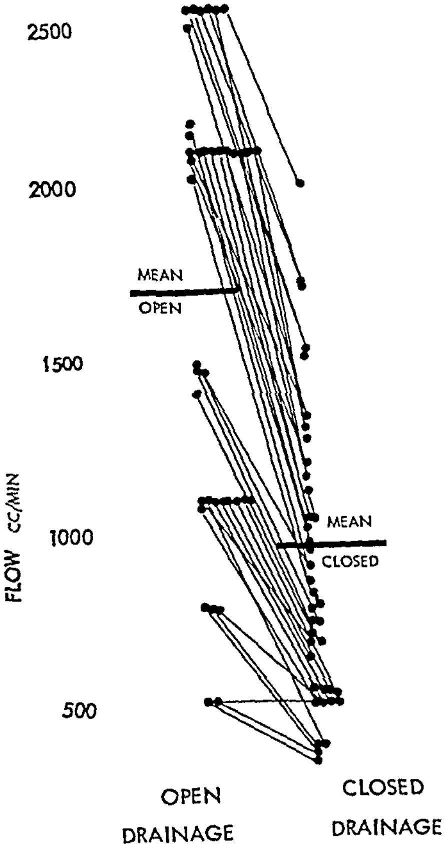

Fig. 2.—Paired flow measurements during open and closed left atrial drainage.

The carotid artery pressure rose to 260 to 280 mm. Hg and the femoral artery pressure fell to 20 mm. Hg during this same interval. During open bypass, left atrial and pulmonary venous pressures were equal and ranged between 10 to 0 mm. Hg. Pulmonary artery pressure was unchanged. Carotid artery and femoral artery pressures were maintained within physiologic limits and varied according to the dog's blood volume and amount of bypass flow. With open left atrial drainage, the reservoir was either raised or lowered until the level remained constant at a given flow setting. If the dog was hypovolemic, left atrial pressure was low and atrial return was diminished. Blood was then added to the system and in this manner the animals tended to regulate their own blood volume The same is true clinically of total cardiac bypass in which the caval blood is drained by gravity Consequently, in these studies, left atrial pressure and bypass flow were regulated by the dog's blood volume Upon switching to closed drainage, left atrial pressure dropped to –10 to –25 mm Hg and occasionally to levels as low as –100 mm Hg The pulmonary venous pressure however, as measured from the wedged pulmonary artery catheter, did not fall, but slowly increased Pulmonary artery pressure remained constant The carotid artery pressure rose and the femoral artery pressure fell (Table I) Interestingly enough, if the flow setting was increased at this time, these differences were often magnified

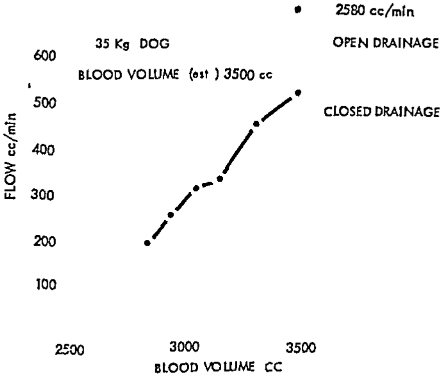

Fig 3 —Influence of blood volume on bypass blood flow during closed left atrial drainage

Table I Successive Pressure Readings During Thoracic Aorta Cross Clamping on Changing From Open to Closed Left Atrial Drainage During Left Atrial to Femoral Artery Bypass

	OPEN DRAINAGE (2,100 c c /min)	CLOSED DRAINAGE (520 c c /min)
Carotid artery	125/110	170/130
Femoral artery	122/96	96/78
Pulmonary artery	18	18
Pulmonary vein	2	16
Left atrium	2	–12

DISCUSSION

Two mechanisms may be involved during closed left atrium to femoral artery bypass to account for the observed pressure changes The first is collapse of the left atrium due to the negative pressure This was observed readily in these dogs This partially occludes the catheter and limits egress of blood from the left atrium The second is probably the partial or intermittent obstruction of the pulmonary veins at the venous atrial junction A valve mechanism

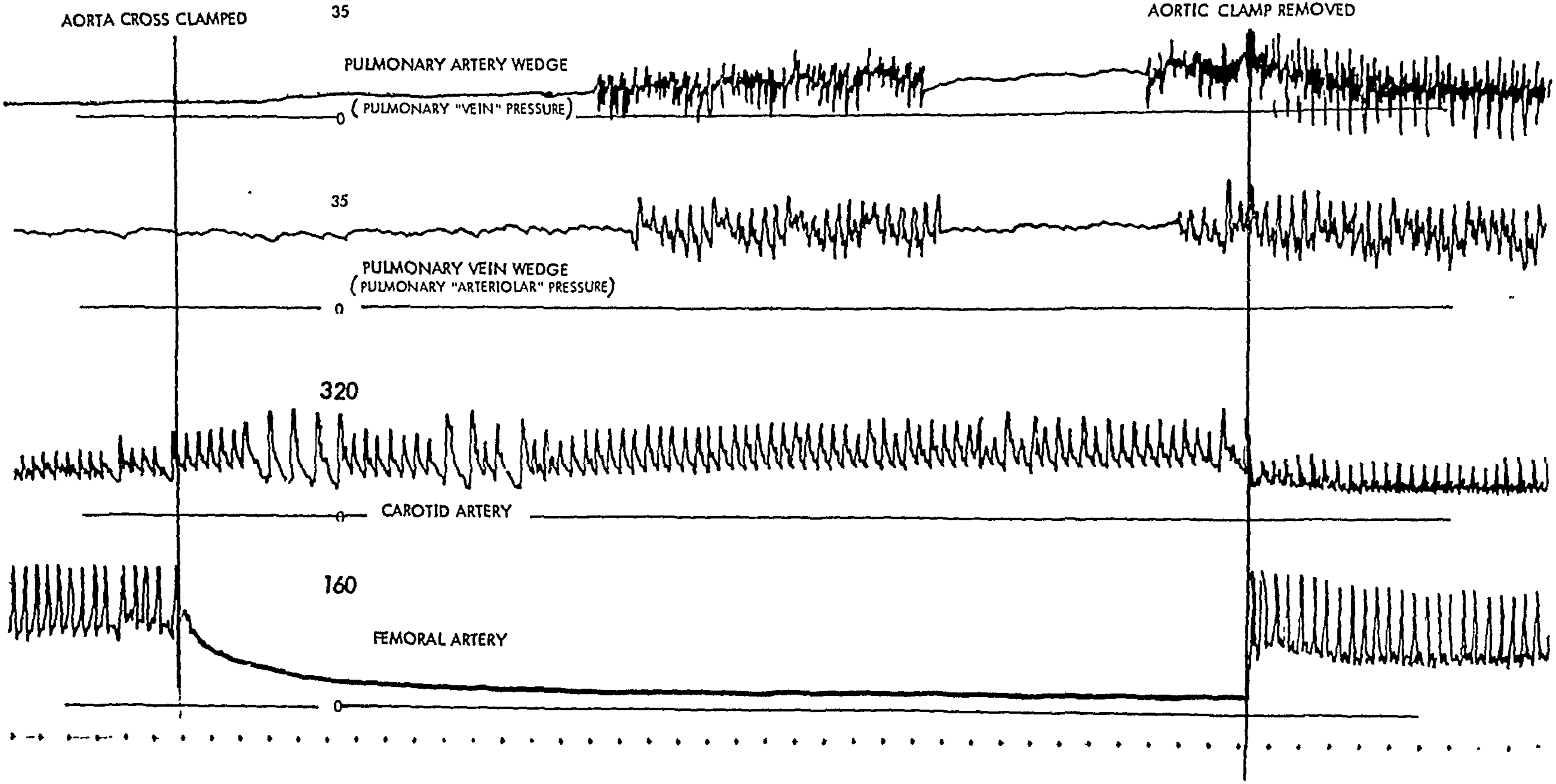

Fig. 4.—Aortic Cross-Clamping Without Vent. Pressure measurements during occlusion of descending aortic arch. (Meaning circuit of oscillograph alternately on and off during pulmonary pressure tracings.)

exists at this junction, for it is known that during normal atrial systole there is very little reflux of blood into the pulmonary veins[3] This is probably the result of the contraction of atrial muscle around the pulmonary venous orifices Similarly, with the application of negative pressure within the left atrium, the atrial walls around the vein orifices may be drawn together, partially or intermittently obstructing pulmonary venous return and resulting in an increase in pulmonary venous pressure

The practical importance of these findings is obvious Closed atrial drainage may yield inadequate proximal decompression and insufficient flows distally Increasing the pump flow setting often magnifies these difficulties The preference for hypovolemia during this period may be disastrous, for it markedly decreases flow The direct relationship between blood volume and available venous return during extracorporeal circulation has been pointed out by others[4, 5]

An additional disadvantage of closed drainage which was encountered in these studies was coronary air embolism, invariably fatal in the 5 dogs in which it occurred This is due to the negative pressure sucking air into the left atrium around the catheter[6] In the dog, this air lodges in the coronary arteries and can be seen in these vessels

Open drainage obviates the dangers which result from attempting to suck blood from a closed system Therefore, during surgical procedures necessitating aortic arch cross clamping at this institution, closed left atrial drainage has been replaced by open, or reservoir drainage

SUMMARY

Comparisons were made between open and closed left atrial drainage, during left atrium to femoral artery bypass, in 13 dogs with thoracic aorta cross clamping At the same pump flow settings, open drainage yielded greater left atrial drainage with larger and consistently reliable flow volumes to the distal aorta These differences were magnified in hypovolemic dogs Mechanisms for differences between open and closed drainage are discussed

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THE DIFFERENTIATION OF ANEURYSM AND MEDIASTINAL TUMOR

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ONE of the most difficult problems facing the thoracic surgeon is the preoperative differentiation of mediastinal masses presenting in the left chest. These are commonly either carcinoma of the left lung invading the mediastinum, aneurysm of the transverse or descending aorta or, last, one of the various tumors that occur in the anterior mediastinum. Usually the anterior mediastinal tumors can be differentiated preoperatively by their position and configuration on the x-ray films. On the other hand, carcinoma of the lung and aortic aneurysm are often confused, short of thoracotomy. Angiocardiography[1] has provided a means of distinguishing these two latter lesions in most cases. However, its use is not infallible and the following cases are presented to demonstrate some of the problems encountered in lesions in this area and how the various special studies now available are used in making a diagnosis.

CASE REPORTS

CASE 1.—M. L. (S.U.H.—No. 359914), a 54-year-old white man, was admitted to the hospital with a 1-month history of cough, fever, and hoarseness. Chest x-ray studies demonstrated a large mediastinal mass which was interpreted as a possible aneurysm (Fig. 1, *A* and *B*). Left scalene node biopsy and bronchoscopy were negative for tumor, but the latter revealed a paralyzed left vocal cord. The serology was negative. Angiocardiography was performed and demonstrated a sharply defined ascending and descending thoracic aorta (Fig. 2, *B*). In addition, it was noted that the left pulmonary artery did not fill, presumably due to impingement of the mass on the vessel. Thus, a preoperative diagnosis of carcinoma of the lung was made. At exploratory thoracotomy an inoperable squamous cell carcinoma of the lung was found.

Comment: Although a pulmonary neoplasm was considered to be the most likely diagnosis before operation, angiocardiography was helpful in ruling out an aneurysm.

CASE 2.—O. D. (S.U.H.—No. 361467), a 51-year-old white man, entered with a 6-week history of weight loss, malaise, and cough. He had been referred to the hospital after chest roentgenograms had been interpreted as follows: "Examination of the chest reveals a large aneurysm of the aorta which originates from the junction of the transverse portion of the aorta and the descending portion" (Fig. 3, *A* and *B*). Physical examination showed some

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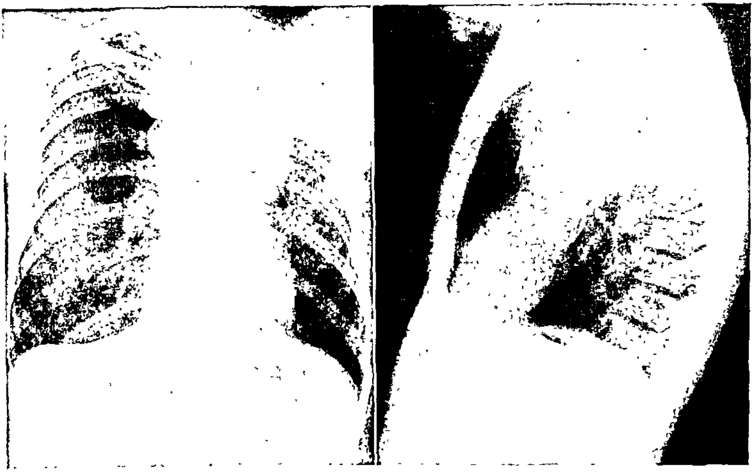
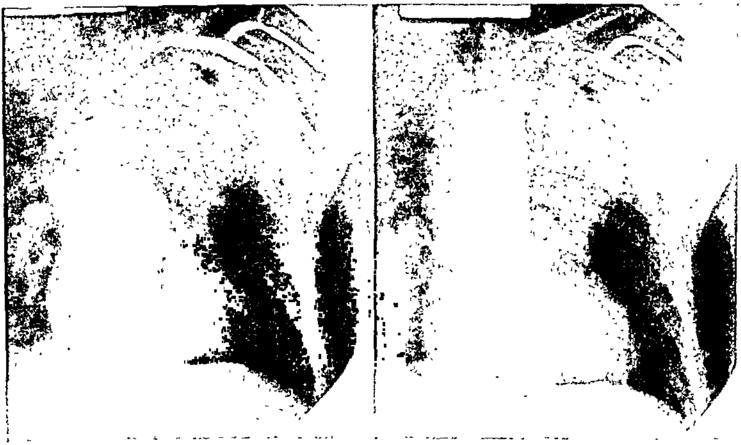


A. *B.*

Fig. 1.—*A*, Posteroanterior chest film of Case 1 which shows a round mass in anterior mediastinum, thought to be an aneurysm. *B*, Lateral chest film of Case 1.

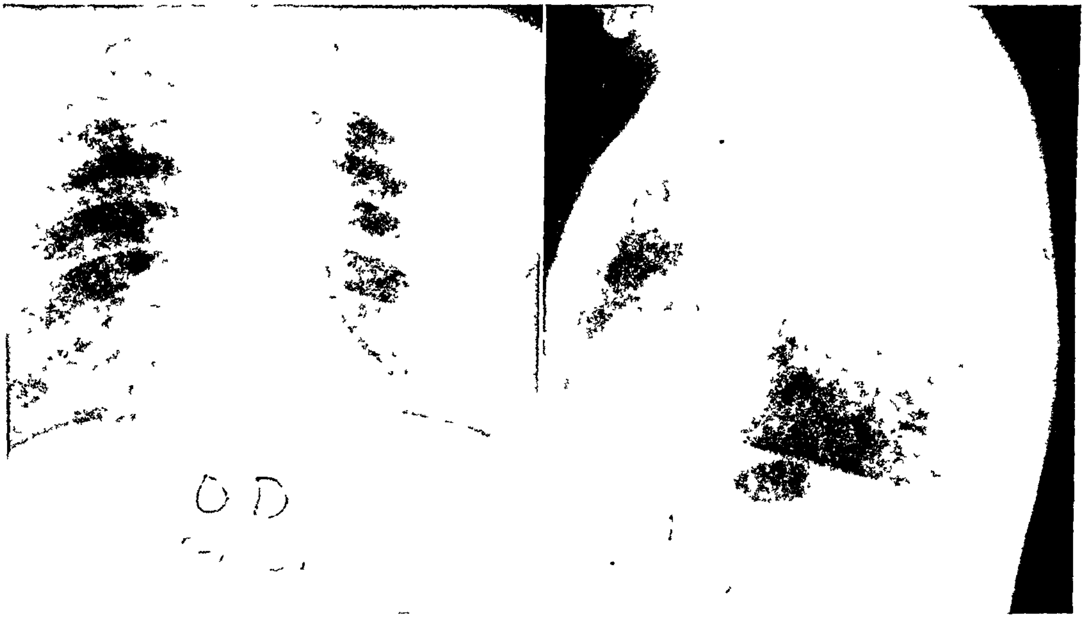


A. *B.*

Fig. 2.—*A*, Angiocardiogram of Case 1 showing absence of filling of left pulmonary artery, presumably due to impingement of the mass on the vessel. The right pulmonary artery is well filled. *B*, Angiocardiogram of Case 1 which shows a sharply defined ascending and descending aorta.

venous distention on the left side of the neck and a palpable left supraclavicular lymph node. The serology was negative. Bronchoscopy and excision of the left supraclavicular node were performed. Anaplastic carcinoma was present in the lymph node. Radiotherapy of the mediastinum resulted initially in shrinkage of the mass.

Comment: This case is of interest since the referring radiologist interpreted the chest roentgenogram as showing an aneurysm. Scalene node biopsy was performed to confirm our clinical diagnosis of carcinoma of the lung. If this had been negative for metastatic tumor, our next procedure would have been angiocardiography.



A. *B*

Fig. 3.—*A*, Posteroanterior chest film of Case 2 which shows a mediastinal mass interpreted as an aneurysm. *B*, Lateral chest film of Case 2.

Case 3.—J. M., a 23-year-old white man, had a routine chest film (Fig. 4) taken which demonstrated an anterior mediastinal mass of undetermined etiology. A history of trauma to the left chest 5 years previously was obtained. Because of the possibility of an aortic aneurysm, he was referred to our hospital for further investigation. A retrograde aortogram was performed which was interpreted as showing that the mass was separate from the aorta (Fig. 5). Subsequent exploration revealed a teratoma of the anterior mediastinum.

Comment: Again a diagnosis of aortic aneurysm was strongly suspected on the basis of the chest films. Retrograde aortography correctly demonstrated that the mediastinal mass was separate from the aorta.

Case 4.—O. H. (S.U.H.—No. 346329), a 59-year-old Negro man, entered the hospital with shortness of breath. He had been treated for syphilis in 1920 and in 1946. On physical examination, he was noted to have a paralysis of the left vocal cord and a systolic murmur in the left fourth interspace. The serology was doubtfully positive. Roentgenograms of the chest (Fig. 6, *A* and *B*) were interpreted as follows, "Huge anterior mediastinal mass with calcific margins. Possibilities are luetic aortic aneurysm, dermoid cyst, or thymoma." After kymograms, the favored radiologic diagnosis was anterior mediastinal cyst, probably dermoid. Since aortic aneurysm could not be excluded, angiocardiography (Fig. 7, *A* and *B*) was

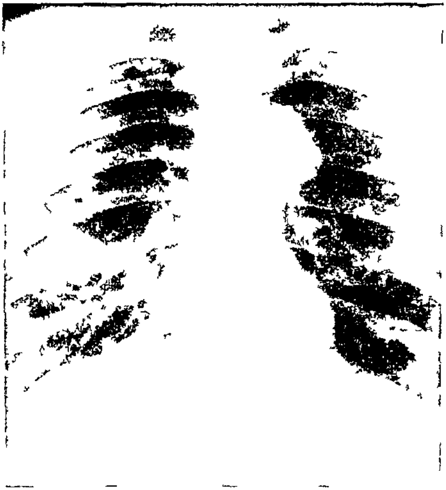


Fig 4—Posteroanterior chest film of Case 3 reported as showing a probable aneurysm

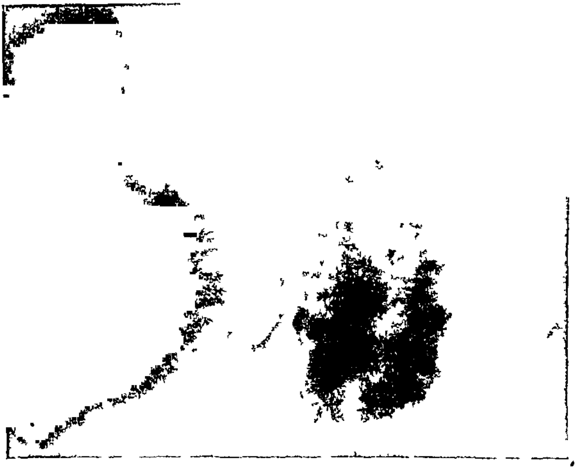
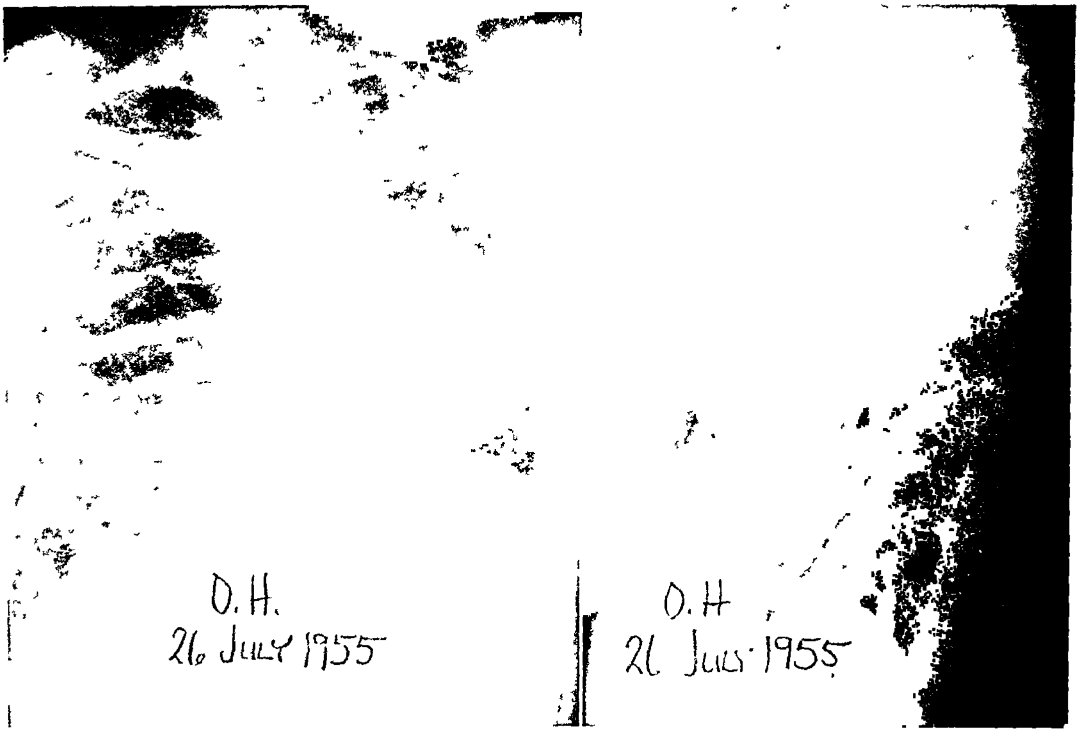


Fig 5—Aortogram lateral projection of Case 3 interpreted as showing that the mediastinal mass is separate from the aorta

carried out. The radiologic report on this examination was, "A smooth walled, normally contoured and normal outlined aorta visualized and there is no evidence of any opacification of the large anterior mass. It is felt, therefore, that the latter is definitely not an aneurysm of the aorta. Some widening at the aortic knob is probably due to inferior dipping and bending of the aortic arch." On the basis of this interpretation, the preoperative diagnosis was changed to cyst of the mediastinum. At exploration, a firm rubbery nonpulsating mass was found. This clot-filled aortic aneurysm was inadvertently entered and the patient died (Fig. 7, *C*).

Comment: This case demonstrates that angiocardiographic findings may be misinterpreted when an aneurysm is filled with clot.



A *B*.

Fig 6—*A*, Posteroanterior chest film of Case 4 The anterior mediastinal mass was interpreted as an aneurysm on the initial films *B*, Lateral chest film of Case 4 which shows that the mediastinal mass is anterior.

CASE 5.—V. D. (S.U.H.—No. E150098), a 53-year-old white man, sought medical advice because of left chest pain. Chest x-ray studies (Fig. 8, *A* and *B*) showed a left anterior mediastinal mass interpreted as a mediastinal tumor. At exploration, the surgeon found an anterior mediastinal mass that he considered to be an aortic aneurysm. The chest was closed and the patient was admitted to Stanford Hospital, service of Dr. Frank Gerbode, for further care. Review of the chest films again suggested a tumor but angiocardiography seemed definitely indicated in view of the exploratory findings. This study disclosed a sharply defined aortic border and appeared to rule out aortic aneurysm (Fig. 9). At a second thoracotomy, the anterior mediastinal mass was found to be an inoperable carcinoma of the lung, proved by microscopic section.

Comment: This case demonstrates the difficulty in distinguishing mediastinal tumors from aortic aneurysm, even at exploration. Angiocardiography was useful here in arriving at a correct diagnosis.

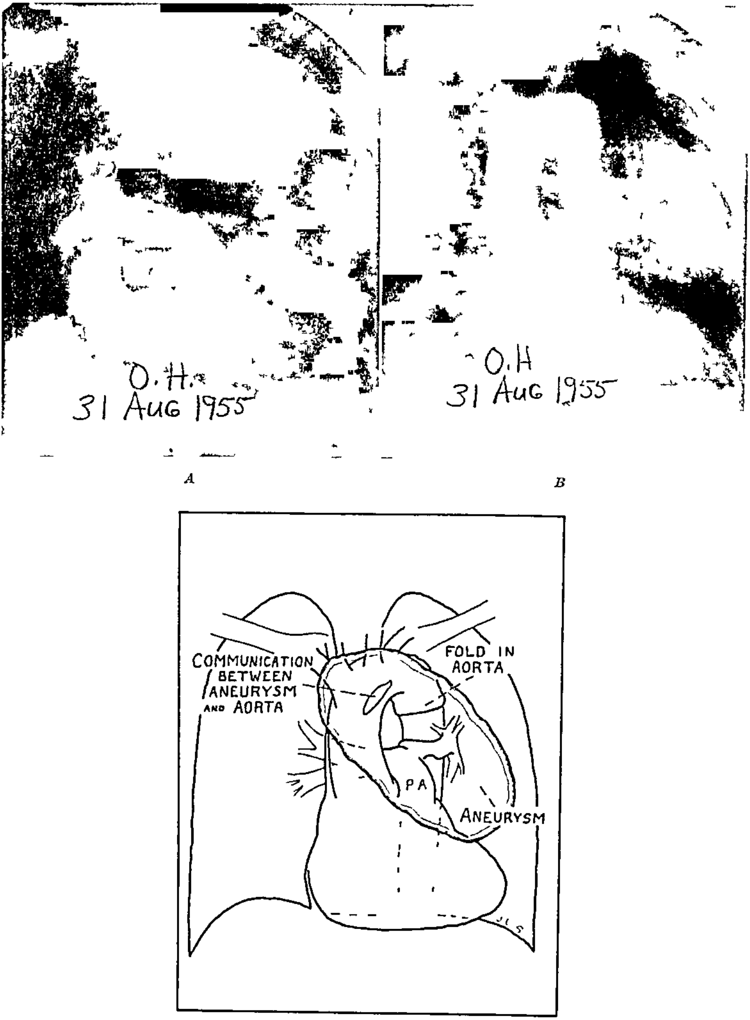


Fig 7 —*A*, Angiocardiogram of Case 4 which shows poor filling and displacement of the left pulmonary artery

B, Angiocardiogram of Case 4 interpreted as showing no connection between aorta and mediastinal mass The tortuosity and folding of the descending aortic arch can be seen Note the aneurysmal dilatation at the point of the take off of the innominate artery from the aortic arch

C, Drawing based on the angiocardiograms of Case 4 and the findings at operation

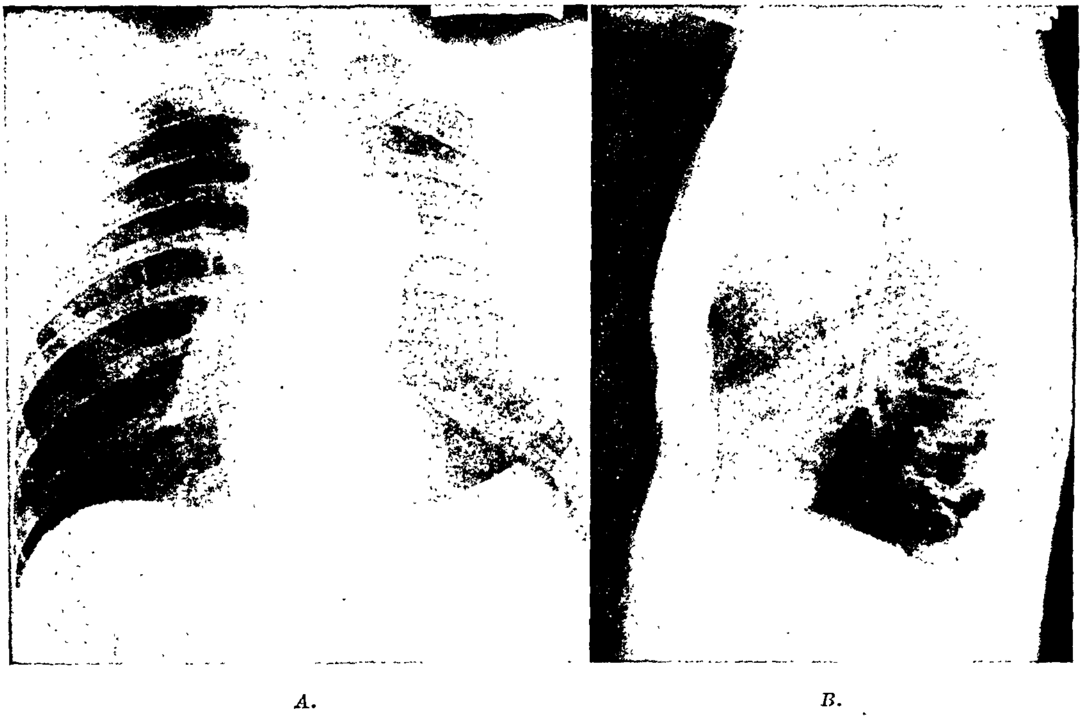


Fig. 8.—*A*, Posteroanterior chest film of Case 5 which shows spherical anterior mediastinal mass with admission diagnosis of an aneurysm of the aorta. *B*, Lateral chest film of Case 5 which shows spherical anterior mediastinal mass.

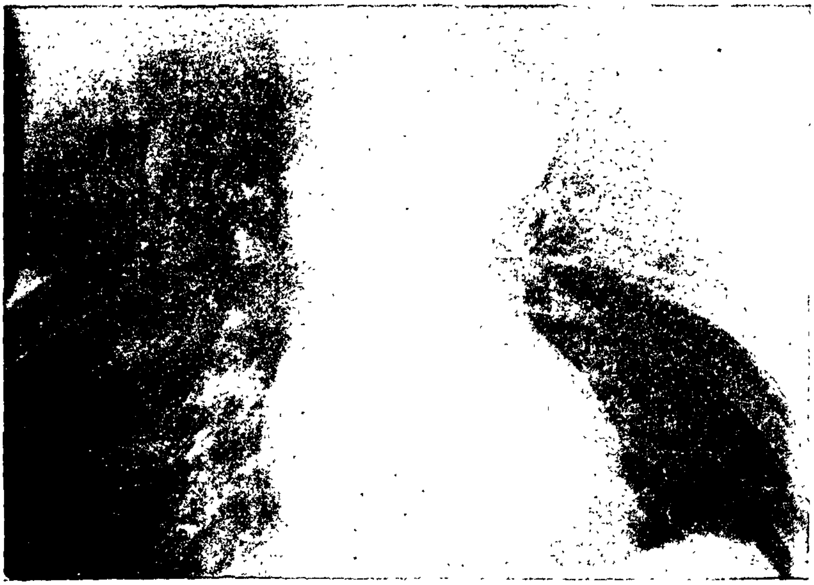


Fig. 9.—Angiocardiogram of Case 5 interpreted as showing that the anterior mediastinal mass is separate from the sharply defined aorta.

DISCUSSION

A correct preoperative diagnosis in these cases is important because special equipment and abilities must be available if an aortic aneurysm encountered at operation is to be dealt with successfully.

Conventional methods of diagnosis include physical examination, chest x-ray studies, and kymography. Fluoroscopy and kymography may demonstrate the presence or absence of pulsation. Nevertheless, these findings may cause confusion, since solid tumors can transmit the pulsations of the great vessels whereas many aneurysms do not pulsate, due to extensive thrombus formation within. Tomography may be helpful in demonstrating whether or not a mass is continuous with the aortic shadow, but it is not definitive.

With the introduction of angiocardiography and aortography it was hoped that this dilemma would be resolved. Although angiocardiography is usually successful in the differentiation of these masses, this is not always true, and, as seen in Case 4, in spite of what appeared to be an adequate visualization of the aorta, an incorrect radiologic diagnosis was made. Because of this diagnosis, the surgeon was not prepared for the possibility of an aneurysm at the time of thoracotomy.

If the mass in question opacifies by angiocardiography or retrograde aortography, the diagnosis of aneurysm is confirmed. However, a negative report is not so conclusive, as many aneurysms do not opacify. Steinberg and Dotter[2] and Sussman[3] have reported cases in which aneurysms did not opacify with angiocardiography, but a correct diagnosis was made because, in one instance, a second aneurysm was present which did fill with dye, and, in the other, the stigmata of syphilitic aortitis were present. These changes of syphilitic aortitis have been described by Steinberg and his associates.[4] They include aortic dilatation, irregularity of the aortic lumen, calcification of the ascending aorta, aortic tortuosity, and abnormal aortic wall thickness. Many of these findings are more easily demonstrated on left anterior oblique or lateral projections of the angiocardiogram. In Case 4, just reported, we do not know whether the aorta was normal or whether its appearance was misinterpreted as being normal.

Perhaps another view, lateral or oblique, would have demonstrated the syphilitic changes in a clearer manner, and might have resulted in a more successful outcome in this case. This case also demonstrates that an aneurysm of the ascending aorta can present on the left side of the chest instead of its usual projection on the right side. Of the various special techniques now available to differentiate carcinoma of the left lung and aortic aneurysm, visualization of the thoracic aorta either by angiocardiography or aortography is the most reliable.

However, we wish to stress that even with utilization of the best diagnostic tools at hand, the surgeon must be aware of the possibility of encountering either lesion at the time of thoracotomy.

SUMMARY

The preoperative differentiation of aneurysm and mediastinal tumor is important because of the difference in the surgical equipment and abilities necessary to treat these two conditions. The diagnosis can usually, but not invariably, be made by contrast visualization of the aorta. Illustrative cases are presented.

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TUBULAR HYPOPLASIA OF A PERSISTENT RIGHT AORTIC ARCH WITH SURGICAL CORRECTION

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AN UNUSUAL anomaly, consisting of absence of the left aortic arch with tubular hypoplasia of a persistent right aortic arch, was recently encountered. A review of the literature has failed to disclose any similar case report. The method of surgical repair will be described and the embryologic derivation of this anomaly will be discussed.

CASE REPORT

A 16-year-old white male was admitted to The Ohio State University Hospital Feb. 15, 1959, with a diagnosis of coarctation of the aorta. He complained of shortness of breath, chest pain on exertion, and cold feet. The past history indicated that for the first 3 months of life he had frequently choked on his feedings. The blood pressure was 178/90 mm. Hg in the right arm, 110/60 in the left arm, and 100/60 in the legs. A Grade 2 systolic murmur was heard in the left second interspace and in the interscapular area. Femoral pulsations were only faintly palpable.

The electrocardiogram suggested left ventricular hypertrophy. A barium study demonstrated a pressure defect in the posterior wall of the esophagus, suggesting the presence of an anomalous vessel (Fig. 1). The usual left aortic arch indentation of the esophagus was absent as noted in Fig. 2. Instead, the esophagus is displaced to the left.

Operative Findings.—The chest was entered through a left posterolateral incision. The descending aorta was slightly to the right of its normal location. Its proximal end gave rise to a diminutive left subclavian artery (Fig. 3, *D*). There was no evidence of any connection to a left aortic arch. The pericardium was then opened and an enlarged ascending aorta was found. The first branch was the left common carotid, the second was the right common carotid, and the third was the right subclavian artery. At first, it appeared that the ascending aorta ended in these three branches, but further dissection disclosed another branch, approximately the diameter of the carotid vessels (6 to 7 mm.), arising from its posterior wall. This rudimentary right arch passed behind the esophagus and joined the descending aorta 3 cm. distal to the origin of the left subclavian artery. The ascending aorta was markedly pulsatile, whereas the descending aorta pulsated weakly. A ligamentum arteriosum arose from the left pulmonary artery and joined the descending aorta on the anteromedial surface of its saccular termination.

Operative Repair.—A curved vascular clamp was applied to the medial aspect of the ascending aorta parallel to the long axis of the vessel to exclude a portion of its wall

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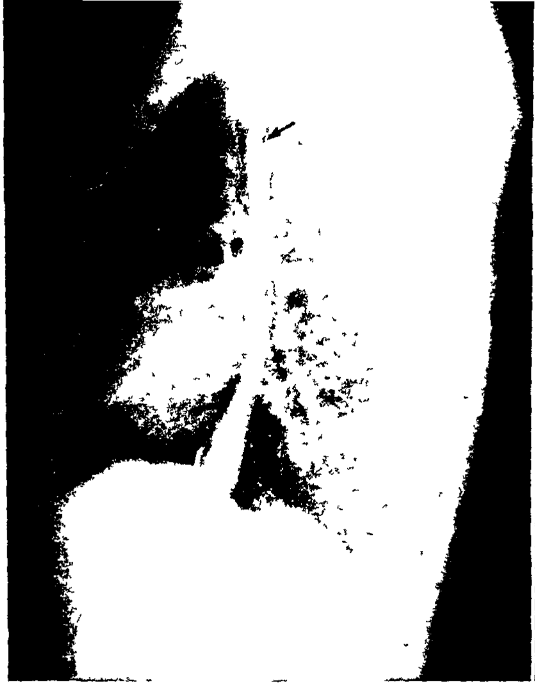

Fig. 1

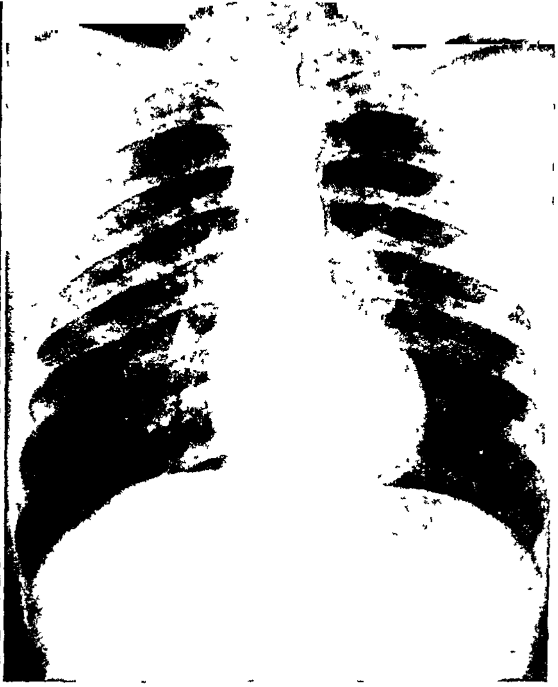

Fig. 2.

Fig. 1.—A left lateral chest roentgenogram demonstrating a pressure defect in the posterior wall of the esophagus caused by the hypoplastic right aortic arch.

Fig. 2.—The esophagogram demonstrates an absence of the usual indentation of the left wall of the esophagus by a left aortic arch. Instead, the esophagus is displaced to the left.

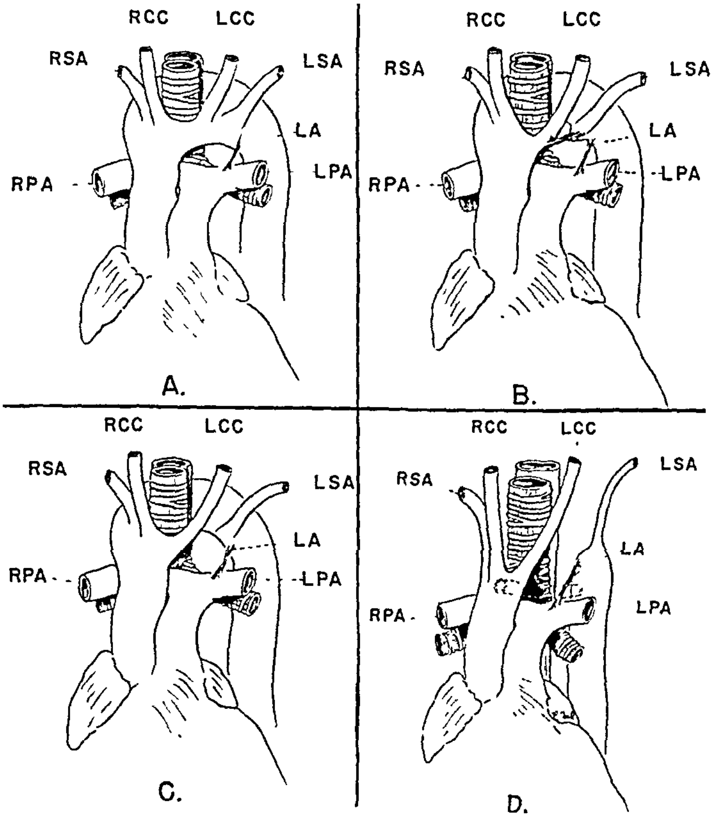

Fig. 3.—These drawings illustrate the successive steps in the derivation of tubular hypoplasia of a persistent right aortic arch. Starting with a functional double aortic arch (*A*), atresia occurs in the left arch between the origins of the left carotid and subclavian arteries. The atretic segment may remain as a fibrotic cord (*B*), or may completely disappear (*C*). Tubular hypoplasia of the right arch has occurred simultaneously (*D*). The left subclavian artery arises from the descending aorta.

Care was taken not to obstruct the flow of blood from the left ventricle. Another clamp was applied in the same way to the descending aorta. A crimped Teflon graft, $\frac{5}{8}$ inch in diameter, was anastomosed in end-to-side fashion to a longitudinal incision placed in the excluded portion of each vessel. A continuous 5-0 arterial suture was used (Fig. 4). This resulted in the formation of a vascular ring surrounding the esophagus and trachea, but care was taken to employ a graft of sufficient length to prevent pressure on these structures.

The patient's postoperative course was uncomplicated. Three months after operation the blood pressure in the arms was 150/100 mm. Hg and 148/110 in the legs. A faint systolic murmur remained audible.

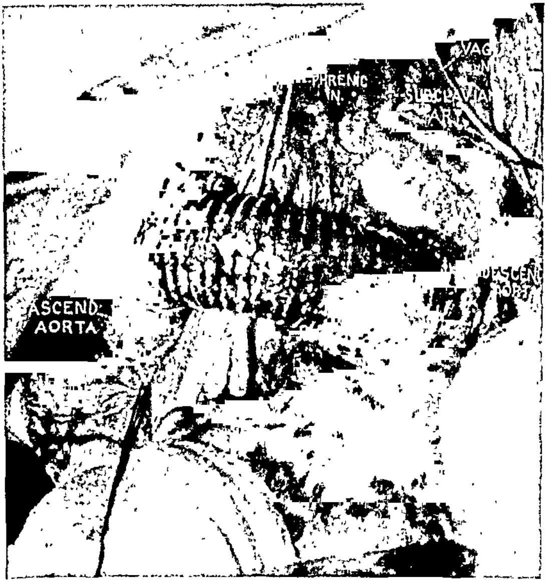

Fig 4.—Operative photograph of the anomaly after completion of the Teflon graft anastomosis.

DISCUSSION

To understand this anomaly, a review of the normal embryology of the aortic arch is helpful.[1] Six pairs of branchial arches appear at different times in embryonic life (Fig. 5). The first, second, and fifth arch on each side disappear. The third aortic arches persist as the common carotid arteries. The right fourth arch forms the proximal portion of the right subclavian artery *(a)* while the segment between the subclavian artery and the dorsal aorta *(b)* disappears. The left fourth arch forms the portion of the adult aortic arch *(c)* between the origin of the left common carotid and the entrance of the ductus arteriosus *(d)*. The ventral part *(e)* of the right sixth arch becomes the right pulmonary artery and the dorsal part *(f)* disappears. The ventral part of the left sixth arch *(g)* forms the left pulmonary artery, while the dorsal part remains as the ductus arteriosus *(d)*.

The derivation of aortic arch anomalies may be best understood, as suggested by Edwards,[3, 4, 5] by referring to a functional double aortic arch as the basic pattern (see Fig. 3, *A*). Such a functioning double arch does exist at one stage of fetal life.[3]

If atresia of the left fourth arch occurs, it usually involves that portion between the left subclavian artery and the insertion of the ductus arteriosus. However, the atresia may occur between the left carotid and left subclavian arteries (see Fig. 3, *B*). In this event, the latter vessel arises from the descending thoracic aorta. If the atresia occurs late in fetal life the atretic segment remains as a fibrotic cord. If the atresia occurs at an earlier stage, as in the case presented, no connection between the vessels may be found (see Fig. 3, *C*). The innominate artery depends for its existence on the disappearance of the right fourth arch beyond the origin of the left common carotid artery. If *this arch persists,* as *in our case, the right subclavian and common carotid* arteries arise separately (see Fig. 3, *D*).

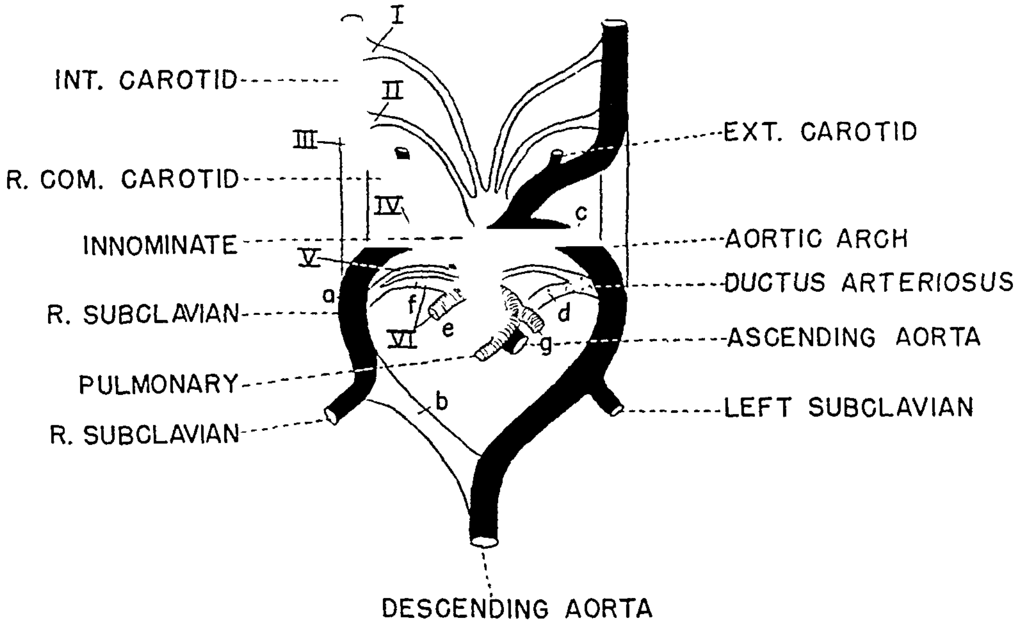

Fig. 5.—A diagram of the six pairs of embryonic aortic arches. The vessels outlined in solid black persist while the vessels in white disappear. The ductus arteriosus (*d*) is stippled to indicate persistence until after birth.

Edwards has used the term "tubular hypoplasia" to describe cases in which there was a uniform narrowing of a long segment of a left arch. This is to be distinguished anatomically from coarctation with a short segment of stenosis. Both conditions may result in the same functional disturbance. The term "infantile coarctation" has been loosely applied to any narrowing of the aorta proximal to the ductus whether it be a true coarctation, a hypoplastic segment, or an area of atresia. Tubular hypoplasia most frequently involves that portion of the left arch between the left carotid and the left subclavian arteries. To the best of our knowledge, tubular hypoplasia of the right arch has not previously been recorded.[6] The present case should be properly referred to as one of tubular hypoplasia of a persistent right arch.

Baffes[2] has suggested the use of homologous aortic grafts to correct such defects in which primary resection and anastomosis is impossible. In experimental work on dogs he successfully placed a graft from the side of the ascending aorta to the side of the descending aorta. He found that if the aortic arch was very narrow as in coarctation, or if it were tied off, the graft remained open. However, if the aorta was wide open and the graft was nonobligatory, it tended to shrink and close off within 3 or 4 months. In the present case the hypoplastic right arch was markedly diminished in cross-sectional area and it is expected that the graft will remain open as an obligatory one. It was known to be functioning well 4 months after surgery.

SUMMARY

A previously unreported type of congenital aortic arch anomaly is described. This consisted of an absent left aortic arch and tubular hypoplasia of a persistent right arch. The condition manifested itself clinically as coarctation of the aorta. The embryologic derivation of this anomaly and the method of surgical correction are described.

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PLICATION OF THE AORTIC RING IN THE CORRECTION OF AORTIC INSUFFICIENCY

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IT SHOULD be technically possible to diminish effectively the cross-sectional *area of the aortic ring, by approximately one third, by plicating the area of the* noncoronary cusp. This conversion of the valve to a bicuspid configuration, without interference with the coronary circulation, might be of benefit in cases of free aortic insufficiency associated with aneurysmal dilatation of the base of the aorta. The validity of these assumptions has been explored by a series of animal experiments, and in one human case.

EXPERIMENTAL OBSERVATIONS

Sixty-two unselected, apparently healthy, mongrel dogs averaging 20 kilograms in weight were utilized in this study. All operations were perfomed under anesthesia maintained by a standard veterinarian solution of Nembutal administered intravenously. Right thoracotomy through the fourth interspace was performed, and respirations were maintained by a pump, rhythmically delivering oxygen under positive pressure through an endotracheal tube. The pericardium was incised vertically, anterior to the right phrenic nerve, and the pericardial flaps were held apart with traction sutures. Umbilical tapes were placed about the superior and inferior venae cavae and ascending aortic arch, respectively, and the azygos vein was ligated in continuity. The right auricular appendage was retracted laterally and inferiorly by means of a traction suture attached to its tip, exposing the base of the aorta in the region of the noncoronary cusp (Fig. 1).

A curved De Bakey clamp was placed on the right anterolateral wall of the ascending aorta and a longitudinal incision, approximately 2 cm. long, was made extending from the base of the aorta distally, in the portion of the aortic wall within the clamp. Inflow occlusion was then produced by tightening the umbilical tapes around the venae cavae, followed by occlusion of the aortic arch. At this point, the De Bakey clamp was removed, and a long curved clamp was inserted through the aortotomy toward the aortic valve. The mouth of the

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clamp engaged one of the valve leaflets and avulsed it With some experience, it was possible selectively to avulse the noncoronary cusp Inflow occlusion was then discontinued and, as blood welled up through the aortotomy incision, the De Bakey clamp was replaced, followed by release of aortic arch occlusion

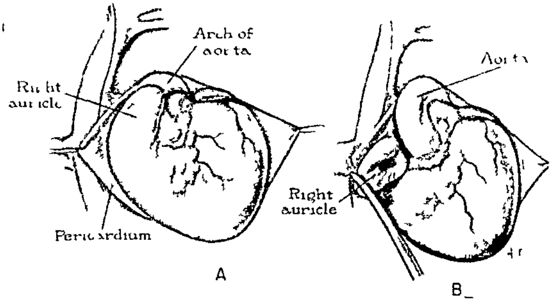

Fig 1—*A* and *B* Exposure of the noncoronary portion of the base of the aorta

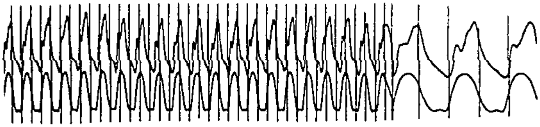

Fig 2—Dog No 59 Pressure curves from aorta (*upper tracing*) and left ventricle (*lower tracing*) following the creation of aortic insufficiency Note the high amplitude of the aortic curve which equals the left ventricular pressure curve amplitude which indicates marked degree of insufficiency

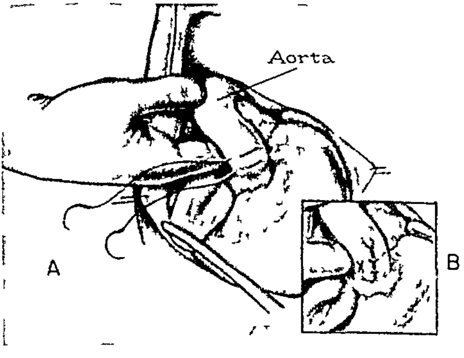

Fig 3—Technique for insertion of deep mattress sutures into aortic wall at the base of the aorta over the noncoronary cusp area

The aortotomy was closed with a continuous over-and-over suture of 5-0 arterial silk. The hemodynamic effect of the valve leaflet avulsion was evaluated by means of simultaneous pressure curves obtained from the left ventricle and ascending aorta and comparing these with similar pressure curves obtained from identical areas prior to creation of the lesion. In the majority of dogs, a definite insufficiency pattern was obtained following creation of the lesion (Fig. 2).

Fig. 4.

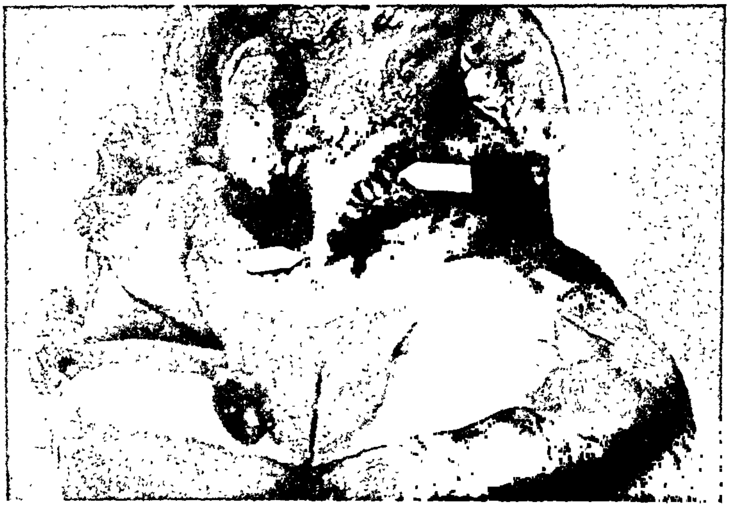

Fig. 5.

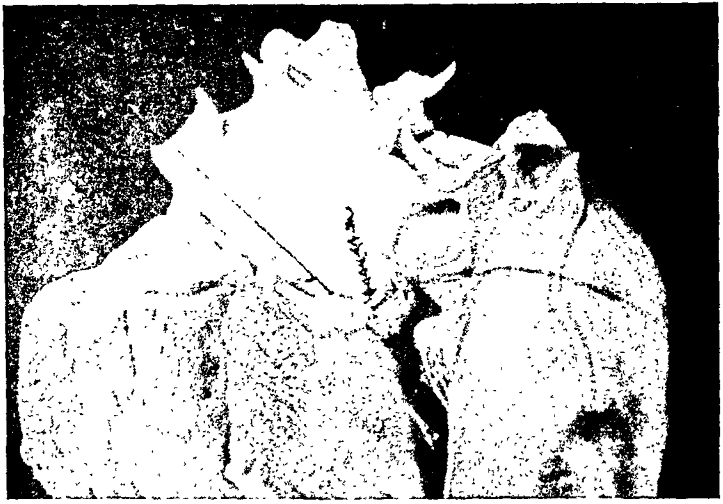

Fig. 4.—Dog No. 59. Autopsy specimen which shows the sutured aortotomy incision which had been utilized to avulse a leaflet (*upper arrow*), and a pleating mattress suture (*lower arrow*) inserted in an attempt to correct the lesion.

Fig. 5.—Inner aspect of base of aorta following attempted correction pleat.

In the last 15 dogs, an attempt was made to correct the aortic insufficiency immediately following its creation. After the aortotomy wound was closed and the pressure curves were obtained, inflow occlusion of the venae cavae was reinstituted. With the operator's left index finger in the transverse sinus elevating the base of the aorta, one or two large mattress sutures were placed in the aortic wall overlying the noncoronary cusp (Fig. 3). As these sutures were tied, a large pleat was produced in the aortic wall, in many instances decreasing the circumference of the aortic valve annulus by one third Figs 4 6 demonstrate the appearance of a maximal correction pleat, and the sutured aortotomy incision Following placement of the sutures, inflow occlusion was terminated and, once equilibrium had been established, pressure curves were obtained from the left ventricle and ascending aorta In spite of the placement of the maximal pleats, the pressure curves repeatedly failed to show any significant change in the insufficiency pattern

CLINICAL EXPERIENCE

Plication of the aorta in the region of the noncoronary cusp thus proved to be ineffective when applied to the correction of acute aortic insufficiency produced by avulsion of the valve cusp in dogs On the other hand, a favorable clinical response with a similar method in cases of aortic insufficiency associated with a dilated aortic ring had been reported by Creech[2] with cardiopulmonary bypass and by Hufnagel[6] with a closed technique The combination of severe angina, free aortic regurgitation, and a hugely dilated aorta comprised the indications for this operation in the following case

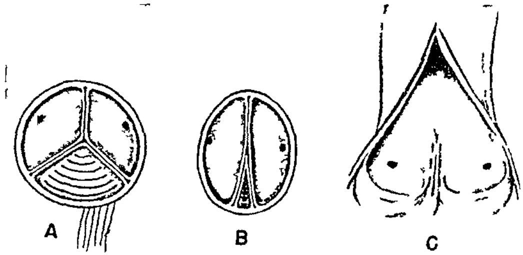

Fig 6—Diagrammatic reconstruction of plication of area of noncoronary cusp

CASE REPORT

G M, Admission 103408, a 49 year old Negro male garage attendant, was admitted to *the Montefiore Hospital on Jan 26, 1959*, with a chief complaint of angina pectoris of increasing severity, and shortness of breath when lying down Penicillin had been administered in large dosage shortly prior to hospitalization, when a blood Wassermann test had been found to be positive, he had received no previous treatment, but recalled a penile lesion in his youth There was no history of rheumatic fever

Three years prior to admission the patient developed severe pressing anterior chest pain on exertion and severe shortness of breath when lying flat At this time he consulted a physician who prescribed nitroglycerin tablets, digitalis of unknown dosage, and diuretics which had been used intermittently The patient experienced relief of the angina with the use of nitroglycerin, however, his consumption progressively increased to as many as one tablet per hour while working During the course of the past 3 years the patient had had ankle edema on at least one occasion which was relieved by an intramuscular diuretic

On examination the patient was noted to be a well-developed Negro man who was ambulatory and appeared in no acute distress. The pulse was 88 and regular; blood pressure 180/44 mm. Hg. There was a visible pulsation accompanied by a thrill over the suprasternal notch and bilateral supraclavicular areas. The heart was enlarged to the left, with the point of maximal impulse in the sixth interspace at the mid-clavicular line. All heart sounds were diminished and replaced by loud systolic and diastolic murmurs loudest at the aortic area and transmitted to the apex and right chest. These were accompanied by systolic and diastolic thrills over these same areas, as well as over the carotid, subclavian, and femoral arteries. Liver and spleen were not palpable. An asymptomatic umbilical hernia was noted. There was no ankle edema or clubbing. Neurological examination revealed a slight anisocoria, the right pupil being larger than the left; the right knee jerk was greater than the left.

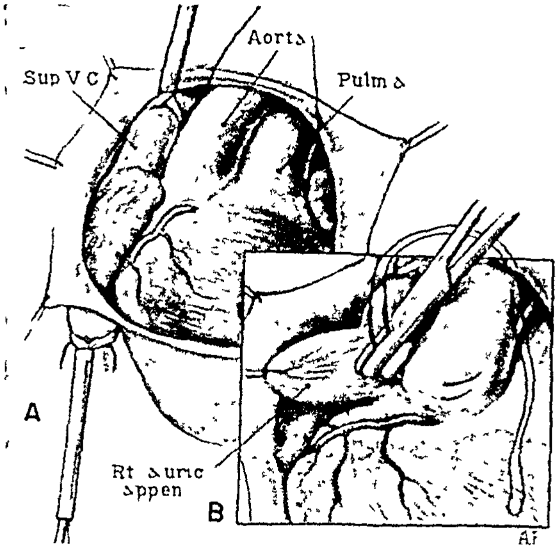

Fig. 7.—Placement of a horizontal mattress suture in one stroke by simultaneous passage of both needles.

Cardiac fluoroscopy disclosed an expansile fusiform aneurysm in the ascending aorta up to the first portion of the arch, with 3+ enlargement of the left ventricle. Electrocardiography showed regular sinus rhythm, with an enlarged left ventricle. The electroencephalogram was normal. The roentgenograms showed marked uncoiling of the aorta, with aneurysmal dilatation of the ascending portion and calcification in the arch. Secondary enlargement of the left atrium and left ventricle was present. The blood serology was positive, with 3+ flocculation and 4+ Kolmer tests. The spinal fluid serology was negative. The venous pressure was 82 mm. of water, with no rise on right upper quadrant pressure. The Decholin circulation time was 18 seconds, arm to tongue.

Plication of the base of the aorta was performed on March 4, 1959. Under satisfactory general intratracheal anesthesia, with a cannula in the left saphenous vein at the ankle, the patient was positioned with the right side of the chest slightly elevated. A right submammary incision was made, and the right pleural cavity entered in the third interspace. There was a generalized diffuse adhesive pleuritis, making it difficult to enter the right pleural cavity. The incision was extended medially, above the left nipple, the left pleural cavity entered in the second interspace, and the sternum was transected with a Lebsche knife. The remnants of thymus were mobilized from the anterior surface of the pericardium, and the pericardium was opened widely, through an incision extending vertically in front of the right phrenic nerve and extended horizontally across the base of the heart. Tapes were passed around the superior vena cava and inferior vena cava, intrapericardially.

The aorta was huge, measuring 5.5 cm. in diameter just above the valve ring, and widening slightly a short distance above this. The right coronary artery was greatly dilated and tortuous. The branches of the left coronary artery were similarly enlarged. The base of the aorta was mobilized on its right lateral and posterolateral aspects, exposing the very base of the noncoronary sinus of Valsalva. With short periods of venous inflow occlusion, none of which extended over 45 seconds in length, a series of 6 horizontal mattress sutures was passed through the noncoronary cusp area, in an attempt to narrow the base of the aorta. The suture material was 1-0 silk, with large curved atraumatic needles on each end of the silk,* passed on a needle holder especially prepared to hold both needles at once, and previously threaded through an Ivalon pillow (Fig. 7). None of the sutures was tied until they had all been placed. During the process of passing these sutures, the heart rate became grossly irregular and finally practically stopped. Intermittent cardiac compression was instituted and the heart went into ventricular fibrillation. While intermittent compression was continued, the sutures at the base of the aorta were all tied anteriorly, over Ivalon pillows. The heart was then defibrillated with electric shock, two shocks at 50 volts being ineffective, and a third shock at 100 volts arresting the heart, from which it was massaged back into a strong effective beat. Two additional sutures were placed in the plicated area of the aorta, deeply, where a strong thrill could still be felt (Fig. 8).

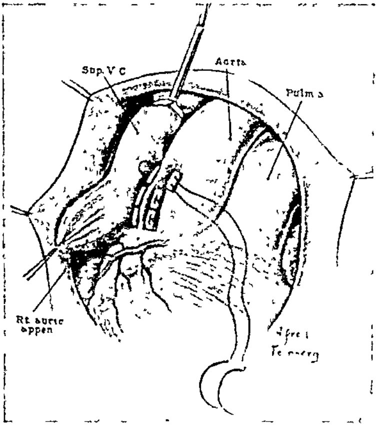

Fig. 8.—Ridge produced by plication of noncoronary cusp area at base of aorta.

The blood pressure changed from the precorrection level of 160/30 to 130/70 mm Hg. Pulse tracings in the aorta after plication showed a flattening of the dicrotic notch, as compared with preplication (Fig. 9). The plicated base measured 4.4 cm. in diameter, in contrast with 5.5 cm. preoperatively; this effectively reduced the cross-sectional area at this level by approximately one third.

The pericardium was closed loosely. The interspaces were closed with pericostal sutures, with a tube brought out from each pleural cavity in the fifth interspace for underwater drainage. Three sutures of O braided wire were placed to unite the divided ends of the sternum. Closure of the musculature and subcutaneous tissues was accomplished with running chromic sutures, and of the skin with running silk sutures. The patient received 3 units of blood during the operation, and his condition at the end of the operation was reasonably good. He reacted completely a short while after operation and showed no evidence of cerebral damage from either his short periods of cardiac inflow occlusion or the period of cardiac resuscitation.

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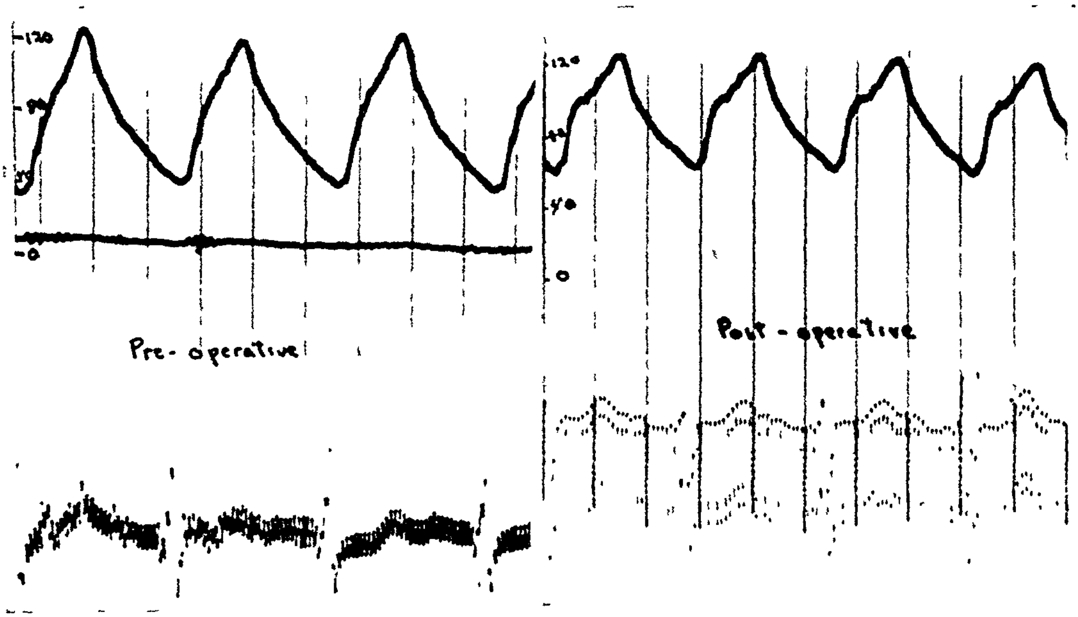
*Supplied by the Ethicon Suture Laboratories, Inc., New Brunswick, N. J.

Immediately on return to the recovery room the patient had a blood pressure of 240/100 mm. Hg which gradually came down and stabilized within 5 hours at 130/70. Chest drainage in the first 24 hours was 1,250 c.c. and the patient received 1,500 c.c. of whole blood. On the first postoperative day the blood pressure was 200/? and pulses developed a ''pistol shot'' character. Symptomatically the patient had no complaints. On the second postoperative day a totally irregular pulse was noted with a rate of 138. The electrocardiogram was interpreted as showing a paroxysmal auricular tachycardia and the patient was started on a rapid digitalization schedule. Venous pressure at this time was 130 mm. of water and circulation time was 22 seconds, as compared to a preoperative venous pressure of 80 and circulation time of 18 seconds. The tachycardia continued with blood pressure maintained at 150/60-40, and quinidine sulfate and potassium chloride were added to the therapeutic regimen. On the third postoperative day the electrocardiogram showed an auricular flutter with 3:1 block. On the fourth postoperative day the blood pressure was 160/74-50 with a sharp diastolic change at 74. The patient continued to be comfortable and complained of no anginal attacks.



A. B.

Fig. 9.—Aortic pressure curves before (*A*) and after (*B*) plication operation in case of human aortic insufficiency.

The tachycardia continued unabated despite use of apparently adequate doses of digoxin, Cedilanid, and Quinidine until March 14. On the ninth postoperative day the ventricular rate slowed to 80, and the electrocardiogram showed atrial flutter. On March 17, 1959, the patient's heartbeat converted to a sinus tachycardia with a ventricular rate of 100, and the course was benign until discharge on April 3. Prior to discharge the blood pressure was essentially the same in both arms, recumbent and sitting, at 140/44 mm. Hg.

When measured 3 months postoperatively the blood pressure was substantially unchanged. The patient could walk 12 to 20 city blocks, in part up hill, without shortness of breath or angina, and had taken no nitroglycerin since the operation.

DISCUSSION

Open heart surgical techniques undoubtedly will provide the optimum solution ultimately of the problems of aortic regurgitation Bicuspidization of the valve with cardiopulmonary bypass has been reported by Bailey,[1] Garamella,[4] and Hufnagel[6] and their associates for palliation when a dilated aortic ring has been the dominant feature Efforts at complete valve replacement by a variety of prostheses when the cusps have been destroyed, have been described with some clinical success by Lillehei[7] and by Hufnagel[6] Both of these types of open procedures while clearly indicating the path for the future, must still be considered in the light of the high operative mortality and the short follow up periods of observation in the survivors The technique of Gadboys and coworkers[3] for visualization of the aortic valve without occlusion or bypass merits investigation This widespread concentration of effort reflects the general disinclination to accept the Hufnagel valve, as inserted into the aorta distal to the origin of the left subclavian artery, as an appropriate answer to the problem

Cases of aortic insufficiency suitable for attempted correction by the plication procedure, while comprising a small percentage of the total, may be selected by appropriate radiologic studies which demonstrate a dilated aortic annulus The ominous prognosis of this lesion when associated with severe angina pectoris is a strong indication for palliative surgery

Four technical details in the plication operation, as described here, merit emphasis

1 Excellent exposure of the noncoronary cusp area at the base of the aorta may be obtained by adequate dissection and mobilization The boundaries of the cusp itself often stand out clearly, and the origin of the right coronary artery is an additional important landmark anteriorly

2 Short intermittent periods of venous inflow occlusion permit placement of the plication sutures in a collapsed aorta, with insignificant blood loss

3 The principle of passing both needles simultaneously for each mattress suture accomplishes two objectives (a) the 2 component parts of each suture are fixed in a more accurate relationship to each other than would be possible if they were passed separately, and (b) the time for passing each suture (and of each period of venous inflow occlusion) is effectively shortened to about one half of that consumed when each needle is passed separately The needle holder designed for this purpose has a short copper shelf on one jaw, and is described in detail in a separate communication [5] * Passage of these sutures was greatly facilitated by standing on the left side of the operating table, and applying the sutures posteriorly anteriorly

4 The hazard of having the sutures erode through the aortic wall may be minimized by tieing them over bolsters on each side of the aorta Ivalon proved to be completely satisfactory for this purpose If the bolster intended for the

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*Supplied by Codman and Shurtleff Inc Boston Mass posterior side of the aorta is placed a short distance back of the 2 needle points, it will help to steady them in the grasp of the needle holder, and will come to rest against the posterior aortic wall when the suture has been passed.

The significance of the relief of angina in the present case, as manifested by discontinuance of nitroglycerin and increased activity by the patient, is difficult to evaluate, particularly in view of the failure to maintain a substantial measurable correction of aortic valvular function as manifested by the wide pulse pressure. Reported relief of angina following a wide variety of procedures emphasizes the unreliability of this criterion. The phase of subjective improvement attendant upon the episode of hospitalization may be properly discounted only after a prolonged period of postoperative observation. The initial reaction to this procedure, however, must be reported as favorable, and may be attributable to increased coronary flow associated with the change in contour of the aortic valve ring.

SUMMARY

1. Plication of the aortic ring has failed to correct aortic insufficiency produced acutely in dogs by avulsion of the noncoronary cusp of the aortic valve.

2. Plication of the noncoronary cusp area at the base of the aorta has been accomplished in a clinical case of free aortic insufficiency associated with dilatation of the aorta, with subjective improvement in the early postoperative course (to date).

3. The principle of simultaneous passage of two needles, swaged onto opposite ends of a strand of silk, permits accurate placement of a horizontal mattress suture in a minimum of time.

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ADDENDUM

April 11, 1960. It is now 13 months postoperatively. The patient has taken no nitroglycerin since operation, and walks stairs without dyspnea. The physical signs of free aortic insufficiency are still present.

MITRAL COMMISSUROTOMY IN PREGNANCY

A Study of 37 Surgical Cases

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R. Gentilli, M.D., and P. N. Siliquini, M.D., Turin, Italy*

Pregnancy in patients with mitral stenosis always presents to the cardiologist and to the obstetrician many puzzling problems: Will there be any serious risk for the mother during the course of pregnancy? In which conditions is therapeutic abortion indicated? Are there some clinical data on the basis of which it is possible to foresee the behavior of the circulatory system during the following months? Finally, what are the indications and contraindications for a mitral commissurotomy?

Cardiac surgery, greatly developed in the last years, has definitely given the opportunity for a new approach and, often, a solution of these problems. The first results of valvulotomy for mitral stenosis, mostly concerning isolated cases, were reported in the literature in 1952: Cooley and Chapman,[11] Logan and Turner,[22] Brock,[9] Baker, Brock, and Campbell,[8] Rummel,[30] Mason,[24] and, in 1953, A. M. Dogliotti, Actis Dato, and Angelino,[16] Sellors and associates,[32] Oselladore,[27] Burwell and Ramsay,[10] and Parkinson.[28]

The first commissurotomy performed during pregnancy was successfully carried out in 1953 by Prof. A. M. Dogliotti and reported by Dogliotti, Actis Dato, and Angelino. In 1954, larger groups of patients were studied by different authors: Crawshaw and associates[12] (12 cases), Watt[34] (7 cases), Haarston[20] (2 cases), Krauss and co-workers[21] (1 case), Provenzale[29] (2 cases), Mendelson[25] (6 cases), Glover and co-workers[19] (5 cases), Tisne[33] (1 case) and Acevedo[1] (2 cases) and their co-workers, Savi and Mezzasalma[31] (6 cases), Marshall and Pantridge[23] (18 cases), Dellepiane (successful operation during an episode of acute pulmonary edema, and report on 21 operated cases), and O'Connell and Mulcahy[26] (emergency successful operation at the end of the pregnancy).

In the Division of Cardiac Surgery of the Surgical Clinic of our University Hospital we have had the opportunity in these last years of studying thoroughly a fairly large number of patients. It is the purpose of this paper to discuss

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from a surgical, hemodynamic, and therapeutic point of view the indications for mitral commissurotomy in pregnancy and to report on the results obtained in 37 patients.

Hemodynamics of Mitral Stenosis in Pregnancy.—

The pathophysiologic dynamics of the circulation in the pregnant woman with mitral stenosis result from the hemodynamic effects of mitral stenosis along with those induced by pregnancy itself (Actis Dato, Angelino and Levi,[4] Siliquini and Revelli[6]):

a. Oxygen-consumption is increased, more or less remarkably in every case.

b. Arterial saturation of oxygen is not significantly varied.

c. The arteriovenous difference of oxygen is always increased, especially during the second part of gestation.

d. The utilization coefficient of oxygen is increased, owing to the synergic effect of pregnancy-factors (increased coefficient at the uterus-level), and mitral defect (reduced cardiac output at the level of the tissues), and higher oxygen utilization, especially during the second part of pregnancy.

e. Cardiac output and cardiac index are reduced.

f. In pregnancy with mitral stenosis, the systolic output should moderately increase, but, on the other side, the mitral defect causes a reduced output so that finally the output appears generally insufficient.

g. The work of the right ventricle is remarkably increased in relation to the degree of stenosis; the work of the left ventricle depends upon the entity *of the defect, but it is generally reduced.*

h. Pulmonary resistances are increased in relation to the mitral defect, the peripheral resistances cannot show important variations or appear slightly increased.

From the compiled data, the conflict between the cardio-circulatory troubles, due to the mitral defect and the necessity of increased work caused by pregnancy, appears rather evident. This is the physiopathologic basis for the considerable deterioration of the circulatory condition which is brought about by pregnancy in patients with mitral stenosis.

MATERIAL

The present study was carried out on a group of 37 women. The ages were between 21 and 43 years; within these limits the patients were very irregularly distributed; however, the approximate mean age was 29 years.

History.—

A definite history of rheumatic fever was present in 9 subjects; in 15, repeated episodes of acute tonsillitis were reported; in 5, there was no evidence of previous rheumatic disease. Peripheral emboli had occurred in 10 out of 37 patients (27 per cent), prior to the time of surgery. Twenty-two patients had had 1 to 4 pregnancies in the past; 6 had had spontaneous abortions; 11 were at their first pregnancy at the time of this study.

The general symptomatology of circulatory insufficiency, such as, dyspnea, easy fatigability, palpitations, episodes of pulmonary edema and/or hemoptysis, etc, had become more evident with the beginning of pregnancy and became worse in the following months.

Clinical and Laboratory Findings—

Auscultation In 19 cases there was the auscultatory and phonocardiographic pattern of pure mitral stenosis—diastolic rumble, opening snap of the mitral valve loud and sometimes split second sound. In addition to these signs, a systolic murmur was present in 5 cases over the pulmonary area, in 4 over the aorta, and in 6 over the mid precordium. On the basis of their aspect and comparison with the other clinical data, these murmurs were considered to be of a functional nature. In 3 cases, a short systolic apical murmur radiating to the axilla suggested the association of a moderate mitral insufficiency.

TABLE 1 – RHEUMATIC HISTORY IN OUR PATIENTS

TYPICAL RHEUMATIC INFECTION	17 CASES
TONSILLITIS	18 CASES
NO RHEUMATIC HISTORY	5 CASES

TABLE 2 – EMBOLIC EPISODES BEFORE OPERATION

BRAIN EMBOLISMS	6 CASES
KIDNEY EMBOLISMS	1 CASE
LIMBS EMBOLISMS	3 CASES

TABLE 3 – PREGNANCIES BEFORE OPERATION

NO PREGNANCIES	IN 11 CASES
FROM 1 TO 4 PREGNANCIES	IN 20 CASES
ABORTION (1 OR MORE)	IN 6 CASES

Electrocardiogram: Thirty three patients had normal sinus rhythm, 4 had auricular fibrillation, 30 out of 37 showed definite evidence of right ventricular hypertrophy.

Roentgenologic findings Standard x ray examination (telecardiogram in the posteroanterior position, right and left oblique views) showed, in most cases, a typical mitral configuration with pulmonary congestion (see Tables I IX)

Surgical Procedure.—

All patients have been operated upon between the third and the seventh month of pregnancy, more frequently during the third or the fourth month.

Operative findings: Thirty-two patients had pure mitral stenosis, in 4 there was some degree of mitral insufficiency, in 1 a moderate aortic insufficiency.

The surface of the mitral orifice was between 0.3 and 1.0 cm.^{2} in 31, and between 1.1 and 1.5 cm.^{2} in the other 6.

TABLE 4 - AUSCULTATION AND PHONOCARDIOGRAM

CHARACTERISTIC FINDING OF PURE MITRAL STENOSIS	19 CASES
FINDING OF PURE M.S. + SYSTOLIC MURMUR IN PULMONIC AREA	5 CASES
FINDING OF PURE M.S. + SYSTOLIC MURMUR ON THE AORTA.	4 CASES
FINDING OF PURE M.S. + SYSTOLIC MURMUR IN MESOCARDIAC AREA	6 CASES
FINDING OF DOUBLE MITRAL DEFECT	3 CASES

TABLE 5 - ELECTROCARDIOGRAPHIC FINDINGS

SINUS RHYTHM		32 CASES
AURICULAR FIBRILLATION		4 CASES
ELECTRIC AXIS	TO RIGHT	29 CASES
	IN MIDDLE POSITION	8 CASES
RIGHT VENTRICULAR HYPERTROPHY		30 CASES

TABLE 6 - ROENTGENOLOGICAL FINDING

STASIS OF PULMONARY VESSELS	(++++)	3 CASES
	(+++)	16 CASES
	(++)	15 CASES
	(+)	3 CASES
ENLARGEMENT OF LEFT ATRIUM	(++++)	4 CASES
	(+++)	16 CASES
	(++)	14 CASES
	(+)	3 CASES
ENLARGEMENT OF PULMONARY ARTERY	(++++)	4 CASES
	(+++)	15 CASES
	(++)	10 CASES
	(+)	8 CASES
HYPERTROPHY OF LEFT VENTRICLE		14 CASES

The edges of the valve were elastic in 25 cases, sclerotic in 9, and widely calcified in 3. In 3, there were auricular thrombi. After the operation the mitral orifice was between 2.1 and 2.5 cm^2 in 4 women, between 2.6 and 3.0 in 15, between 3.1 and 3.5 in 10, and between 3.6 and 4.0 in 8.

Follow up study. Frequent studies at regular intervals have been made for 1 to 5 years after operation.

TABLE 7 – GESTATION PERIOD AT TIME OF OPERATION

Third month	12 cases
Fourth month	18 cases
Fifth month	4 cases
Sixth month	2 cases
Seventh month	1 case

TABLE 8 – INTRAOPERATIVE FINDINGS

Pure mitral stenosis	32 cases
Mitral stenosis with mitral incompetence	4 cases
Mitral stenosis with aortic valvular disease	1 case

	Conditions of the valves
Elastic type	25 cases
Sclerotic type	9 cases
Calcified type	3 cases

Preoperative size of mitral ostiums	
cm^2	Number of cases
0.3-0.4	8
0.5-1	23
1.1-1.5	6

Postoperative size of mitral ostiums	
cm^2	Number of cases
2-2.5	4
2.6-3	15
3.1-3.5	10
3.6-4	8

TABLE 9 –

	Cardio-vascular conditions after operations and delivery
Good or satisfactory conditions	32 cases
Little improvement	5 cases

RESULTS

Maternal Mortality.—No deaths, either during the operation or postoperatively, occurred in this series.

The cardiocirculatory conditions after operations were very markedly or satisfactorily improved in 32 women; in 5, however, a general improvement but a slight exertional dyspnea and palpitation were still present. One of these had an associated aortic insufficiency and the other 4 an associated mitral insufficiency, clinically diagnosed before the operation.

Course of pregnancy and delivery: Thirty of our patients had a normal delivery, 16 of them with forceps, with no complication of cardiac or circulatory insufficiency. Three women recently operated upon were still pregnant at the time this report was written; they are having a normal gestation without cardiac discomfort. In 3, intrauterine death of the fetus followed the operation; 1 patient had a successful cesarean section at the end of a normal gestation.

DISCUSSION AND CONCLUSION

Clinical Observations.—

The embolic episodes before operation have been extremely frequent in this series of patients; the incidence of 27 per cent being higher than that usually found in mitral stenosis (Actis Dato and Weisz,[5] an analysis of 1,074 consecutive cases). This difference is not easily explained since most of our patients were of comparatively younger age and in sinus rhythm. As far as pregnancy is concerned, however, no definite relation appears to be because all reported embolic episodes had ocurred before pregnancy. Another interesting observation was the fact that 26 of our 37 patients had had in the past one or more pregnancies, most frequently followed by a normal delivery; however, the last pregnancy was accompanied by a more or less marked aggravation of their clinical symptoms. In fact, deterioration of the clinical condition of the patients, with increasing palpitation, dyspnea, frequency and severity of attacks of pulmonary edema or hemoptysis, was noted at the beginning of the last pregnancy.

We can state that most of the women subjected to mitral commissurotomy in our Centre came to the hospital not only on the advice of the physician but mainly because of the severe impairment of their cardiac status, which they had not experienced in the previous pregnancies. Other patients whose previous pregnancies had to be interrupted came to the cardiac surgeon with the hope of being cured and becoming able to carry on normal gestation and delivery.

The causes responsible for the aggravation of the clinical symptoms of mitral stenosis during pregnancy are several and complex. The increased load on the heart imposed by the changed metabolic conditions, oxygen consumption, and cardiac output plays evidently the most important role. However, another important factor is probably the increased water retention, due to hormonal influences, which can further aggravate the phenomena of stasis and congestion. We wish to emphasize finally that in most of our cases there was a very tight mitral orifice; it is reasonable to assume that in these subjects with cardiac conditions already impaired that the load imposed by gestation will cause most severe signs of insufficiency.

In 14 cases there was a systolic murmur but no valvular defects could be demonstrated by hemodynamic or clinical data, nor by observations at operation. In fact, most of the murmurs disappeared or were greatly reduced after commissurotomy or after delivery. They are very likely due to the decreased circulation time and do not pathogenetically differ from those in many other physiopathologic conditions, such as hyperthyroidism or anemia. We wish to emphasize the importance of these murmurs, which are very frequent in the pregnant women. A correct recognition of their functional (or inorganic) nature is necessary in order to obtain an exact diagnosis.

The majority of our patients (32 out of 37) were in sinus rhythm; the percentage of auricular fibrillation (about 12 per cent) is definitely much lower than those in the general population who have mitral stenosis who undergo surgical treatment. The reason for this discrepancy is probably that all our patients were of a comparatively younger age and did not show important myocardial damage.

In all of 32 subjects with pure mitral stenosis, x-ray examination had shown some degree of left ventricular enlargement. This phenomenon is probably related to the circulatory changes which take place during gestation, since cadiac rate, at least at rest, does not show considerable modifications. An increase in cardiac output can only be accomplished by an increase of stroke volume, hence of the size of the heart.

In the study of our patients we have paid considerable attention to the problems of the choice of the safest time for operation: 30 patients were operated upon in the third and fourth months of pregnancy, while in the other 7, operations were done in the fifth, sixth, and seventh months.

Some cases have been reported in the literature (O'Connell,[26] Marshall and Pantridge[23]) in which a successful commissurotomy was performed as late as the eighth and ninth month. In our own experience, however, the best period for operation is the fourth month and, actually, it should be performed as soon as possible.

In no case was there a complication of postoperative recurrence of rheumatic fever. According to some authors the endocrine changes occurring during pregnancy act favorably in preventing rheumatic manifestations.

Our patients who had been operated upon were kept under careful medical control and continued digitalis treatment. After a complete cardiological and obstetrical follow-up study through gestation, delivery, and puerperium, we may state that pregnancy by itself does not increase in any way the risks, the difficulties, or the complications of mitral commissurotomy.

Indications for Mitral Commissurotomy During Pregnancy.—

On the basis of our data it is possible to establish some criteria which will help the cardiologist and the obstetrician to solve this important problem, which they always have to face.

1. The knowledge of the cardiac status during previous pregnancies is an indirect datum of great help in the prognosis of the disease during the present gestation; a history of previous pregnancies without any sign of cardiac or

circulatory failure may orientate the physician toward medical rather than surgical treatment, which is, on the contrary, indicated if cardiac abnormalities develop.

2. A progressive deterioration of cardiac conditions before and/or during gestation is a definite indication for prompt surgical treatment.

3. The sudden occurrence of an attack of pulmonary edema is usually a symptom of the downhill tendency of hemodynamic conditions and is therefore a clear-cut indication. In one of our patients an emergency operation was performed at the third month during an acute attack of pulmonary edema which promptly ceased at the moment the mitral orifice was dilated.

4. In cases of combined valvular lesions (associated mitral and aortic lesions associated stenosis, and insufficiency of the mitral valve), the problem of surgical treatment is always very difficult even in the absence of a pregnancy, and needs a careful consideration of every single situation, possibly before pregnancy begins. If an aortic stenosis is associated with mitral stenosis, a combined mitral and aortic valvotomy can be advised and successfully perfromed. If, on the contrary, a severe aortic or mitral insufficiency is associated, the chances of successful medical treatment of an already failing heart are very small. It is also extremely difficult to evaluate the possibilities of continuing a normal gestation, and of accomplishing a normal delivery without danger to the mother. The prognosis of these patients will certainly improve when a reliable method of surgical repair of the combined lesions is possible.

5. We think it is a good policy to perform the operation even in the mild case. The aim of cardiac surgery must be, in fact, not only to cure the established symptoms, but also to prevent the occurrence of future manifestations, which can appear in the last half of pregnancy, particularly during the delivery.

It can conclusively be stated that commissurotomy must be advised and performed without irrational doubts or fears in every case of pure mitral stenosis, the best time being the first months of gestation.

Mitral stenosis is not an indication for a therapeutic abortion.

SUMMARY

Clinical and instrumental findings in 37 women operated upon by mitral commissurotomy during pregnancy are reported.

The maternal mortality was zero, and immediate and long-term clinical results were satisfactory. Three postoperative abortions occurred at various intervals after the operation.

The hemodynamic conditions in pregnant women with mitral stenosis are described in detail on the basis of the writers' personal observations.

The criteria for the evaluation of the indications for mitral commissurotomy during pregnancy are discussed.

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EXPERIMENTAL DELAYED OCCLUSION OF THE LEFT CORONARY ARTERY

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SURGICAL THERAPY for coronary artery disease has met with two imposing problems. On the experimental side, there has been confusion and conflicting evidence on the type of experimental occlusion and consequently there has been inconclusive assessment of the value of an experimental "therapeutic" procedure. On the clinical side, the disease is a potpourri, and case selection, as well as evaluation of therapy, has revolved around the symptom of angina pectoris (the number of attacks, the quantity of nitroglycerin used, etc.), or the presence of historical and electrocardiographic evidence of prior myocardial infarction. Assessment of the patient with angina is enigmatic and judgment of the prognosis of the individual patient in the second group, for purposes of evaluation of any therapy, has proved difficult and requires a large number of cases as seen in the decoagulant studies of recent years.[1]

We feel that the group of patients undergoing acute critical infarction and not responding to medical therapy, who usually die, would constitute an evaluable set of patients if treated and preserved by surgery (almost certainly of the direct type). It might be noted that the effect of the direct surgical attack in the chronic case is presumptive and has not been properly tested in the experimental animal.

The appropriate test animal would be one undergoing a coronary occlusion that is fatal within a few days, and preferably occurring in the awake, closed-chest subject.

Acute ligation of the anterior descending branch of the left coronary artery has been used as a standard and is said to result in a 70 per cent mortality in dogs.[2] However, studies in various laboratories have shown wide variance in results, with mortality ranging from 0 to 100 per cent.[3] The differences are apparently due to many factors: site of ligation, inclusion of the main septal branch, anatomic variations, antecedent medication (especially atropine), anesthesia, etc.[4] In order to minimize some of the variables, slow occlusion in an

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unanesthetized animal with a closed chest has been introduced and used more widely This preparation should give more consistent results in addition to more nearly simulating coronary artery disease in man Many methods have been employed to produce a slow occlusion multiple acute ligations[5], application of silver clips[3, 4], encompassing the artery with periosteum,[6] cellophane,[7] bakelite rings,[7] silver bands[3, 8], spring clamps with jaws separated by catgut[9], screw clamps left inside the chest[10, 11], screw clamps[12, 13], or snares[14] with a controlling device implanted under the skin, radioactive material[15], injecting sclerosing or fibroplastic agents[16], and cannulating with a small polyethylene tube[17] Most of these slow occlusions have been applied to one of three coronary arteries right, circumflex left, or anterior descending left

This laboratory has been interested in the direct surgical approach to the problem of coronary artery disease rather than the introduction of multiple small new channels[18] Slow occlusion of the main stem left coronary artery seemed to offer a major site of occlusion, segmental in nature, and a coronary artery of adequate size for application of some form of direct surgical approach would remain The length of the main stem left coronary artery, before it divides *into the anterior descending and circumflex rami, is less than 1 mm in some dogs* and as long as 4 mm in others The method of occlusion must be tailored to these anatomic limits The purpose of this paper is to describe the method evolved and the subsequent results

In 1956, Berman[19] introduced Ameroid, a casein plastic which has the property of absorbing water when bathed in a salt solution and thus slowly expanding in tissue He produced gradual vascular occlusion in a number of vessels including the coronary arteries Litvak, Siderides and Vineberg[20] made sleeves of Ameroid and placed them around the anterior descending and circumflex branches of the left coronary Since we were interested in occluding the main stem artery, the use of Ameroid in sleeves was impossible

METHOD

Young adult, healthy, mongrel dogs, weighing 11 6 to 21 8 kilograms, were anesthetized with intravenous veterinary pentobarbital sodium and intubated with a cuffed endotracheal tube Respiration was controlled by manual compression of an inflated bag which delivered 100 per cent oxygen in a closed circuit McKesson system containing a carbon dioxide absorbent With the right side down, the left hemithorax was entered through the fourth or fifth intercostal space The pericardium was incised anterior and parallel to the phrenic nerve A traction suture was placed in the left auricular appendage and the pulmonary artery was gently displaced anteriorly The epicardium and fat were incised to expose the main stem of the left coronary artery Number 4-0 silk on an atraumatic needle was passed around the main stem by passing the blunt end of the needle first so as to avoid piercing the artery or its septal branch Care was taken to pass the suture as close to the aorta as possible This suture was tied to a No 0 black silk ligature which was then pulled through (Fig 1) A wafer of Ameroid, 5 mm in length, 6 mm in diameter, and grooved on two sides, was then tied down over the main-stem left coronary artery (Fig. 2). The pericardium and chest were closed in routine fashion; tube suction drainage of the pleural cavity was performed for 4 to 6 hours postoperatively to insure full re-expansion of the lungs. Broad spectrum antibiotics, usually tetracyclines, were given daily postoperatively.

Fig. 1.

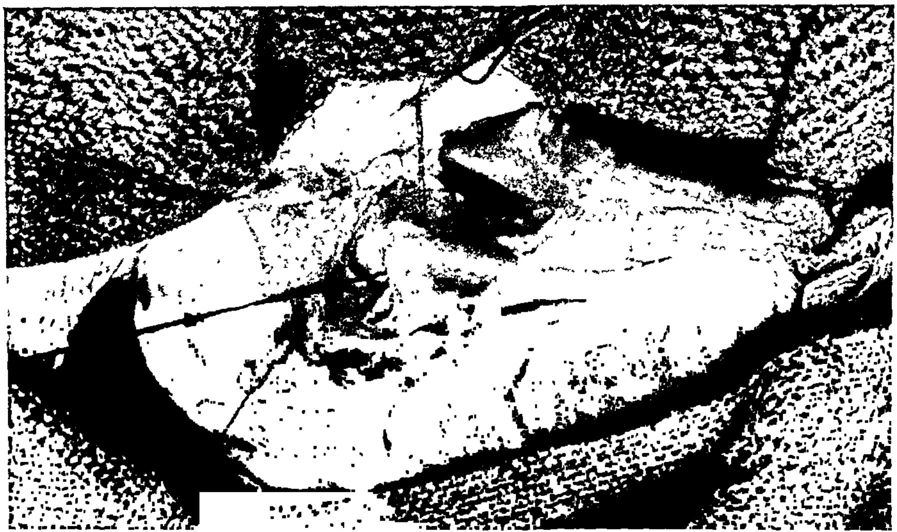

Fig. 2.

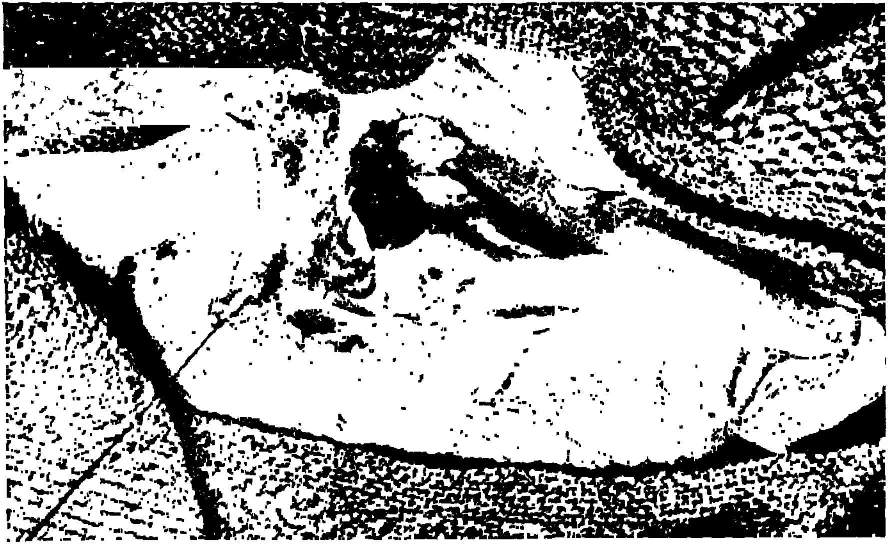

Fig. 1.—The left coronary artery with the ligature in place as seen at operation. The left auricular appendage is retracted to the right. The pulmonary artery is seen above and to the left of the main-stem artery.

Fig. 2.—The Ameroid wafer is tied in place over the main-stem left coronary artery.

RESULTS

Twenty-nine dogs were prepared by the method described. Twenty dogs died between 4 hours and 10 days postoperatively and all exhibited severe occlusion of the main-stem left coronary artery, except 1 which died of pneumonia (Table I). The remaining 9 dogs were sacrificed in 1 month and showed widely patent or minimally occluded main-stem arteries; the Ameroid and ligature were in place, but had not been tied down adequately.

Electrocardiograms were obtained preoperatively, immediately postoperatively, and almost daily thereafter. All tracings were obtained with the dogs in the supine position in order to minimize variations due to positional changes. No animal showed changes diagnostic of myocardial infarction. Transient S-T changes were common. Arrhythmias were common, ranging from ventricular extrasystoles and left bundle branch block to ventricular fibrillation. Terminal ventricular fibrillation was demonstrated in 4 dogs (700, 88, 618, and 152).

The animals were autopsied as soon after death as possible. The diameter of the Ameroid wafer was measured. Approximately one-half of the swelling occurred in the first 24 hours; i.e., 6.0 mm. to 6.7 mm. or an increase of 0.7 mm. (Fig. 3). Because the occluding ligature encircles the wafer, the circumfer-

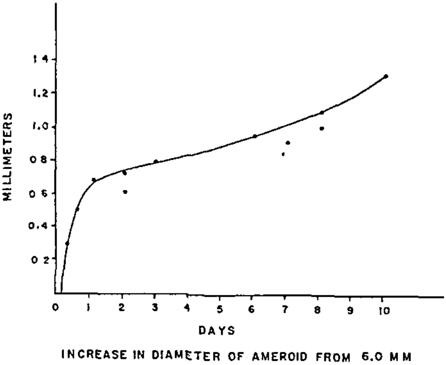

Fig. 3.—Curve showing the rate of swelling of the Ameroid as determined by preoperative and postmortem measurement.

TABLE I. SURVIVAL DATA

DOG NO.	SURVIVAL
520	4 hours
170	1 day
778	1 day
358	1 day
351	2 days
111	2 days
660	3 days
595	3 days
152	3 days
700	5 days
171	6 days
618	6 days
730	7 days
19	7 days
747	8 days
816	8 days
707	9 days
793	10 days
88	10 days

ence rather than the diameter is the effective dimension. The maximum circumferential change was in excess of 4 mm. in 10 days. It can be seen, therefore, that in order to occlude completely the main-stem artery, which has an average diameter of 5 mm., some mild degree of occlusion must be produced by the ligature at the time the wafer is tied in place (Fig. 4). This difficulty was overcome with increasing experience.

A distinct advantage of this method was that an estimate of the degree of occlusion could be made by probing the coronary ostium via the aorta with various sized probes. In the group of animals dying with severe coronary occlusion, 15 had ostia measuring 1.0 mm. or less in diameter; 4 had ostia measuring 2.0 mm. or slightly less. The remaining 10 dogs had widely patent ostia ranging from 2.5 to 5 mm. in diameter; in 1 dog the ligature was distal to the septal branch. All survivors were in the last group.

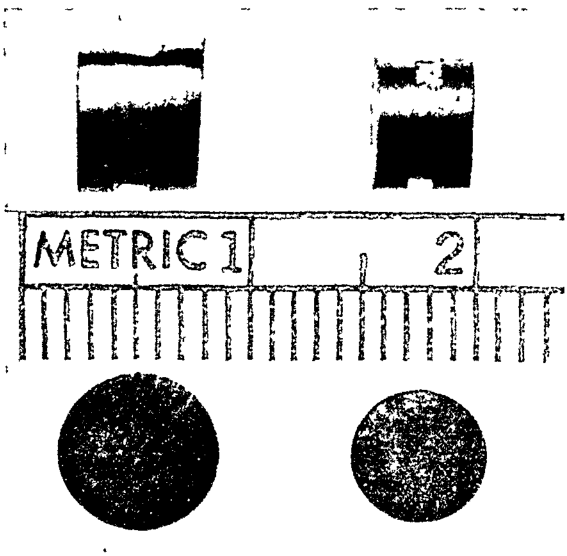

Fig. 4—Photograph showing Ameroid wafer preoperatively (*right*) and at postmortem, 10 days after operation (*left*).

There was no gross or microscopic evidence of myocardial infarction. In one-half of the animals there was histologic indication of varying degrees of pulmonary edema. Sagittal microscopic sections were made through the artery at the site of the occlusion. These sections do not give an accurate account of the terminal degree of patency of the vessel since the Ameroid and ligature must be removed. They show indentation of the wall of the vessel and varying degrees of pressure necrosis; distal organized thrombi and intimal proliferation are seen occasionally (Figs. 5 and 6).

DISCUSSION

The desired 100 per cent lethality was not obtained with this method of coronary arterial occlusion. However, a subject is produced in which treatment by drug or surgery can be tested, since survivors can be checked accurately for left coronary ostium size by transaortic measurement. More importantly, the animals produce the picture of an acute coronary insufficiency within a few days and surgical therapy in this acute stage can be put to trial.

This type of acute, major coronary arterial occlusion is lethal and as demonstrated can be associated with ventricular fibrillation. Murray[21] observed that coronary occlusion results in cyanosis, dilation, and asystole in the area of myocardium supplied by the ligated vessel, and he hypothesized that this results in "paradoxical systole," fall in blood pressure, decrease in left ventricular output, and eventual ventricular fibrillation and death McEachern's studies[22] suggest that the mechanism of ventricular fibrillation may be mediated via the sympathetic nerves from the heart. Beck[23] claims that unequal blood supply

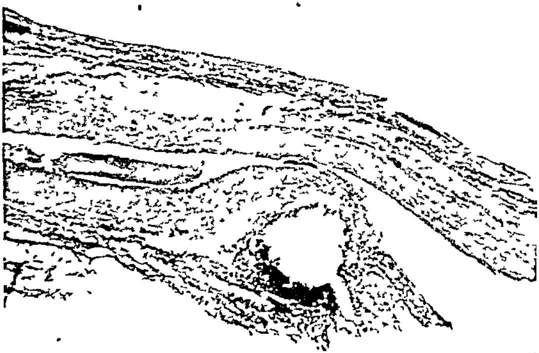

Fig 5

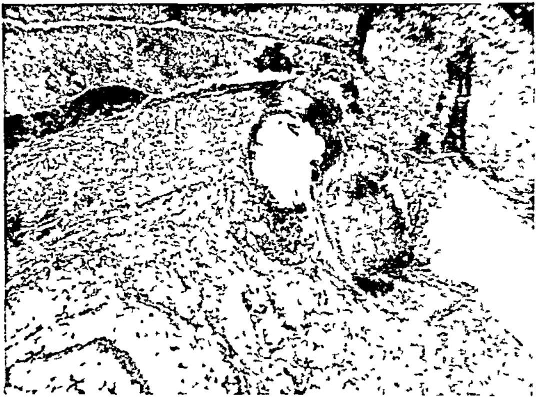

Fig 6

Fig 5—Sagittal microscopic section of the anterior descending branch and main-stem left coronary artery at the site of occlusion There is tenting and pressure necrosis of the vessel wall Organized thrombi can be seen in the anterior descending branch

Fig 6—In addition to the previously noted features, this vessel shows intimal proliferation

and oxygen potentials result in electrical instability and hence ventricular fibrillation.

Because the dog has intercoronary anastomoses to a greater extent than human beings, the use of this animal has been criticized.[24, 25] However, in this subject the potential protection of many of these anatomoses has been obviated by occlusion at the main stem of the left coronary artery. Survival from occlusion at this point has been rare in other studies. Litvak,[20] in slowly occluding the anterior descending and circumflex rami concomitantly, had all 12 dogs die between 4 and 26 days. Lowenfels[9] was able to occlude slowly the main-stem left coronary artery in 12 dogs and all but 1 died within 1 month. In our series, all the dogs with severe occlusion of the main left coronary artery died within 10 days. These animals showed no gross or microscopic evidence of myocardial infarction and can be compared with the group of patients who die soon after an acute episode of coronary insufficiency. Studies are now in progress challenging the usefulness of arterial grafts from the aorta to the circumflex or anterior descending ramus with this method of occlusion. If this is successful, then staged therapy in the post-occlusion period will be attempted. Comparison can also be made with drug-treated, sympathectomized, and decoagulated subjects.

CONCLUSIONS

1. Occlusion of the main-stem left coronary artery has been produced in the awake, closed-chest dog with a simple ligature encompassing the artery and an absorbing plastic wafer (Ameroid).

2. Nearly complete occlusion of the artery results in the death of the dogs in less than 10 days. This is associated with ventricular arrhythmias, but no histologic evidence of infarction.

3. Lethal occlusion was obtained in 19 of 29 animals in this initial series. Degree of occlusion can be measured transaortically and the surviving group can be separated readily with this indicator of failure to occlude the vessel.

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AUTOTRANSPLANTATION OF THE PULMONIC VALVE INTO THE AORTA

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THE SEARCH continues for the ideal aortic valve replacement. Although plastic valves have provided successful palliation in some cases, their usefulness remains limited. Aortic valve homografts were tried experimentally by Hufnagel[1] and by Lam and co-workers[2] who found that normal function of the cusps did not persist. Murray[3] obtained a more favorable impression of valve homografts from his experimental work and reported their use in a few patients with aortic insufficiency. However, collective clinical and experimental experience with vascular homografts suggests that they will ultimately prove unsatisfactory. The disadvantages of synthetic and homograft valves make the use of a valve autograft an attractive alternative. Several reports[4-10] in the literature have indicated that pulmonic valvular insufficiency may be unusually well tolerated; for this reason the pulmonic valve was selected for investigation as an autogenous transplant.

The purpose of this report is to describe an experimental technique for excision of the intact pulmonic valve and its transplantation into the descending thoracic aorta of the dog. This transplantation is accomplished during total cardiopulmonary bypass utilizing anoxic cardioplegia and selective hypothermia of the heart.

METHOD

Healthy adult mongrel dogs, weighing from 13 to 28 kilograms, were anesthetized with intravenous sodium pentobarbital given in a dosage of 30 mg. per kilogram. One hundred per cent oxygen was administered through a cuffed endotracheal tube with an electronic respirator. Each dog was placed on the right side, and a thoracotomy was performed through the left fourth interspace. Pleural reflections in the anterior mediastinum were divided to allow access to the azygos vein and superior vena cava. The azygos vein was ligated and tapes were passed about the extra-pericardial portions of the superior and inferior

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venae cavae. The latter vessel was approached through the pleural reflection inferior to the pericardial sac and anterior to the phrenic nerve. The pericardium was then opened longitudinally anterior to the phrenic nerve, and its edges were sutured to the muscular borders of the incision, thus creating a pericardial well for the heart and eliminating pulmonary tissue from the operative field.

Following the administration of heparin in a dosage of 2 mg. per kilogram, the superior vena cava was cannulated by passing a catheter through the external jugular vein so that the tip lay just proximal to the occluding tape. The inferior vena cava was cannulated through the right atrial appendage. Insertion of the catheter was facilitated by momentarily rotating the heart to the left.

A rotating disc oxygenator* was utilized in all experiments for total cardiopulmonary bypass. A femoral artery and a carotid artery were cannulated and connected by means of a Y adapter to the arterial limb from the oxygenator. Venous return from the venae cavae was collected in a reservoir by gravity flow and supplied to the oxygenator by a rotary pump. During resection of the pulmonic valve, the heart was rendered quiet and dry by occluding the aorta and pulmonary artery with a cloth-covered Satinsky clamp passed through the transverse sinus. Throughout the period of cardiac anoxia, the pericardial well was perfused with a drip of cold isotonic saline, as described in a previous publication,[11] to provide selective hypothermia of the heart. The left heart was decompressed by a left atrial catheter which diverted bronchial drainage into the venous reservoir. Blood pressure was continuously monitored with a cannula in the contralateral femoral artery. Fig. 1 depicts schematically the bypass technique

Following the institution of total cardiopulmonary bypass, the aorta and pulmonary artery were occluded. The pulmonary artery was immediately transected just distal to the valve commissures and any blood remaining in the heart was removed. A small transverse incision was made in the anterior wall of the right ventricular outflow tract a few millimeters proximal to the margin of the anterior cusp. The incision of the myocardium along the cusp borders was then completed under direct vision and the annulus was dissected free of the aorta resulting in removal of the valve intact. Special care was taken to avoid injury to the very adherent aorta and to the anterior descending branch of the left coronary artery which courses in close proximity to the pulmonic annulus. After resection of the valve, the aorta was momentarily unclamped to allow identification of bleeding vessels in the cut myocardium and areolar tissue which surrounded the excised segment of the pulmonary artery. These were clamped and ligated. Any injury to the aorta was also identified and sutured at this time.

Despite the demonstration in early experiments that survival was possible with re-anastomosis of the pulmonary artery to the right ventricular outflow tract, it was subsequently decided that a short length of aortic homograft would

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*Kay-Cross Oxygenator, Pemco Inc, Cleveland, Ohio facilitate restoration of continuity between the right ventricle and pulmonar artery without tension or angulation. Accordingly, a fresh segment of ascending aorta was obtained from a donor animal before each experiment. Th homografts averaged 2 cm. in length and the slightly curved shape seemed appropriate for joining the right ventricle and pulmonary artery. Followin insertion of the homograft, the aortic clamp was removed and the cold salin drip discontinued.

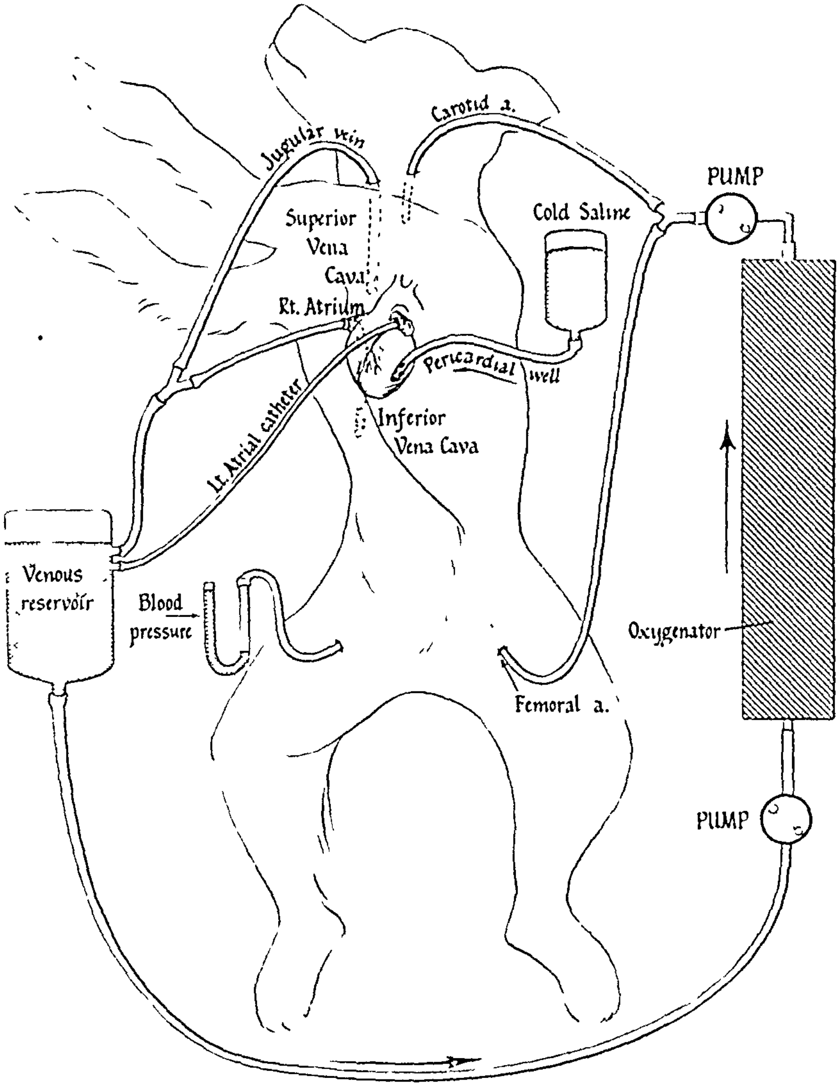

Fig. 1.—Schematic drawing of the heart-lung bypass. The cold saline drip perfuses th pericardial well providing hypothermia of the heart. The left atrial catheter diverts bronchia flow during aortic occlusion.

During the anoxic period, ventricular fibrillation inevitably occurred abou 3 to 5 minutes following aortic occlusion; however, the selective hypothermi rendered the fibrillating heart almost motionless. Following aortic disocclusio the cardiac temperature returned toward normal and the fibrillation becam more vigorous. At this point, gentle massage was administered, followed by electric shock defibrillation In a few instances where defibrillation could not be effected with one or two shocks a small amount of epinephrine was delivered into the left ventricle to induce coronary vasodilatation. Following this maneuver defibrillation was invariably accomplished.

The second part of the operative procedure was carried out during continued perfusion through the carotid and femoral arteries. The descending aorta was dissected free from its bed for a few centimeters distal to the left subclavian artery and divided between two Potts clamps. The excised pulmonic valve was then interposed between the cut ends of the aorta using a continuous suture technique reinforced where necessary by interrupted sutures On completion of these anastomoses, aortic clamps were removed and perfusion was gradually terminated Protamine sulfate in a dosage of approximately 3 mg. per kilogram was administered slowly over several minutes When bleeding seemed satisfactorily controlled, pleural reflections were sutured over the autograft and the chest was closed in layers. Two chest catheters were attached to suction apparatus for several hours postoperatively, and blood replacement was given when necessary. Penicillin and streptomycin were administered over a 5-day period. Fig. 2 illustrates the completed transplantation of the pulmonic valve.

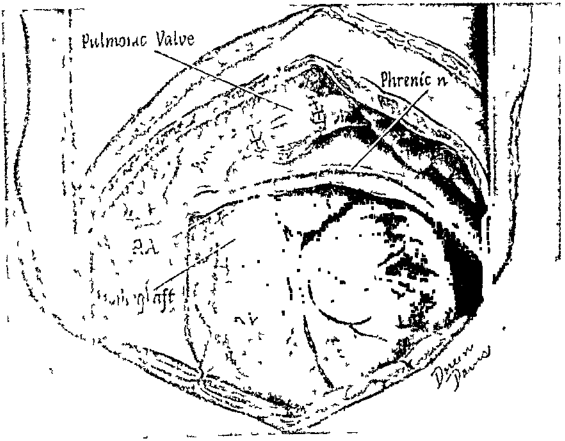

Fig 2—The completed transplantation showing the pulmonic valve in the descending aorta and a small segment of arterial homograft restoring continuity between the right ventricle and pulmonary artery

RESULTS

Thirty dogs were subjected to this operative procedure. The mortality rate was high and uncontrollable bleeding accounted for most of the deaths

It was interesting to note that recovery of the heart from the anoxic period was usually prompt despite absence of the pulmonic valve.

Bleeding came primarily from two sources. During dissection of the pulmonary artery and valve with the aorta occluded, bleeding points were not easily identified. In addition, damage to the root of the aorta where it is fused to the pulmonic annulus was often undetected. Once the segment of homograft was inserted and the aorta unclamped, it was almost impossible to expose the bleeding vessels. The procedure was then changed to include momentary disocclusion of the aorta following excision of the pulmonic valve and annulus. This allowed the bleeding points to be identified and ligated. This momentary unclamping of the aorta at about the 10-minute point in the anoxic period may have served to supply a small amount of oxygenated blood to the myocardium, although this interval of coronary flow was necessarily very brief to avoid excessive blood loss.

The second troublesome source of hemorrhage was the anastomosis between the transplanted valve and the aorta. Technical difficulty resulted from the disparity in diameter, especially between the proximal or myocardial end of the graft and the descending aorta. In addition, the thinner substance of the graft under systemic pressure tended to balloon out between sutures and provide sources of bleeding. It was soon learned that meticulous placement of sutures was necessary to effect a satisfactory anastomosis. This necessitated ong periods of perfusion which seemed uniformly well tolerated. Clotting abnormalities were not apparent in those animals surviving operation.

Another fatal complication of earlier procedures was occlusion of the left anterior descending coronary artery by extensive suturing of the dissected tissues to obtain hemostasis following excision of the pulmonic valve. The subsequent technique of temporary disocclusion of the aorta allowed more precise ligation of bleeding vessels, and the complication of coronary occlusion was usually avoided.

The periods of cardiac anoxia, interrupted only by the momentary unclamping at approximately the 10- or 15-minute point, extended for 30 to 57 minutes. The animals were easily defibrillated and good cardiac action was obtained in all except in the few which had suffered coronary ligation. If subsequent death occurred, it was invariably due to uncontrollable bleeding. In comparison with prior series of animals subjected to comparable periods of anoxia under selective hypothermia,[11] the complete pulmonic valvular insufficiency did not appear to provide an additional burden to the heart during recovery. It was noted that a small area of myocardium about 1 cm. in width adjacent to the anastomosis between the homograft and the right ventricular outflow tract on the anterior surface was frequently infarcted, apparently due to section of a branch from the anterior descending artery. This area has produced no adverse effects.

Table I lists the dogs surviving the operation. The first animal underwent only resection of the pulmonic valve with re-anastomosis of the pulmonary artery and right ventricular outflow tract. When sacrificed at 5 weeks, he appeared well and the heart was of normal size. Three dogs died within the first 2 weeks from aortic rupture at the suture line. This was to some extent anticipated as extensive suturing was often necessary to control bleeding and this may have resulted in necrosis, particularly at the myocardial end of the graft.

TABLE I ANIMALS SURVIVING OPERATION

	WEIGHT (KG.)	DURATION OF CARDIAC ANOXIA (MIN.)	TOTAL PERFUSION TIME (MIN.)	RESULT
1	16.0	32	56	Sacrificed at 5 weeks
2	18.3	41	85	Surviving and well
3	22.3	38	76	Surviving and well
4	15.0	41	97	Died fifth postoperative day, rupture of aorta
5	22.3	38	90	Died at 2 weeks, large pericardial effusion
6	20.0	46	106	Surviving and well
7	17.0	40	90	Died at 3 weeks, large pericardial effusion; transplanted valve appeared normal
8	16.0	43	92	Died ninth postoperative day, rupture of aorta
9	15.1	34	92	Died ninth postoperative day, rupture of aorta, infection at site of rupture
10	27.8	47	114	Died tenth postoperative day, empyema
11	18.0	39	93	Died first postoperative day, hemothorax and atelectasis
12	22.0	42	86	Surviving and well
13	21.2	47	99	Surviving and well
14	20.0	39	95	Surviving and well

The surviving animals appear to be normally active and without signs of heart failure. They will be the subject of further study to determine the ultimate fate of the autografted valves.

DISCUSSION

The question of how essential the pulmonic valve is to normal circulatory function remains incompletely answered. Although isolated pulmonic insufficiency is rarely encountered clinically, the increasing frequency of surgery for congenital pulmonic stenosis raises a practical question concerning the risk of surgically producing pulmonic valvular insufficiency. Accordingly, several investigators have produced varying degrees of experimental, pulmonic insufficiency in attempting to elucidate the significance of this lesion.

Ellison[4] and Ratcliffe[5] and their associates subjected dogs to complete excision of the pulmonic cusps. Their most striking observation was that the animals remained asymptomatic even though some were subjected to regular exercise. The former group presented cardiac catheterization studies which confirmed the presence of free pulmonic regurgitation but demonstrated in all animals normal cardiac output and normal end diastolic pressures in the right

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HEART BLOCK FOLLOWING INTRACARDIAC SURGERY: LOCALIZATION OF CONDUCTION TISSUE INJURY

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HEART BLOCK remains a distressingly frequent complication of intracardiac repair of certain congenital anomalies, particularly ventricular septal defect occurring as an isolated lesion or in such complexes as tetralogy of Fallot and common atrioventricular canal. Several recent studies have demonstrated the anatomic relationships of conduction tissue to various intracardiac defects,[1-4] but no studies have been reported which show the site of injury following operation. The present report deals with the localization of injury to conduction tissue in patients whose intracardiac procedures were complicated by complete heart block.

MATERIAL

Specimens were obtained from 3 patients who had undergone open-heart repair of congenital cardiac defects. In each case complete heart block was observed during or immediately following suturing of the defect, and in each patient heart block was considered to be the primary cause of death.

CASE REPORTS

CASE 1.—The patient was a 5-year-old child who was found to have a heart murmur at 2 months of age, cardiomegaly at 6 months of age, and cyanosis at 2½ years. Cardiac catheterization performed on two occasions was interpreted as demonstrating an atrioventricular canal. At operation, on Oct. 31, 1958, a persistent atrioventricular canal with a large interatrial component, a small ventricular septal defect, and a cleft of the mitral valve were found. These defects were repaired without cardiac arrest. After 33 minutes of perfusion the patient was taken off the pump-oxygenator and heart block was noted. Her immediate postoperative course was complicated by hypotension and respiratory insufficiency. Despite supportive measures her condition deteriorated and she died 20 hours following operation.

CASE 2.—This patient was a 4-year-old child with tetralogy of Fallot who underwent open-heart surgery on Nov. 6, 1958. With the patient on cardiopulmonary bypass, cardiac arrest was induced with potassium citrate. The right ventricle was opened and the ventricular septal defect repaired. An Ivalon patch was placed in the right ventricular outflow tract, extending into the pulmonary artery. After release of the aortic clamp and massage,

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a cardiac beat was observed but the electrocardiogram showed complete heart block Post operatively the patient remained unresponsive and cyanotic Respiratory arrest occurred 3 hours after the conclusion of surgery and was followed by cardiac arrest Despite emergency thoracotomy and massage, the heartbeat could not be re established

CASE 3—On cardiac catheterization of this 7 year old child, a ventricular septal defect, with no evidence of right to left shunt, and a pulmonary artery pressure of 85/40 were demonstrated On March 5, 1959, she underwent repair of the interventricular septal defect At the end of the repair, complete heart block was noted on the electrocardiogram and electrodes were placed in the heart and subcutaneous tissues Following operation her immediate course was satisfactory and the heart rate was maintained by an electronic pacemaker However, during the subsequent 2 weeks her condition deteriorated despite maintenance of the heart rate with the pacemaker She remained in complete heart block and showed evidence of progressive deterioration, with death on the seventeenth postoperative day

METHODS

Each heart was examined and photographed with the area of repair undisturbed Sutures were then removed and the specimens photographed with the defects open From each specimen a block of tissue was removed which completely encircled the defect, including the coronary sinus, the inferior portions of the atrial walls and interatrial septum, and the superior portion of the ventricular walls and interventricular septum This block was sectioned in a direction corresponding approximately to the anterior posterior plane of the body Sections were stained alternately with hematoxylin and eosin and Masson's triple stain Graphic reconstructions of the conduction system were made following histologic study of the slides

OBSERVATIONS

Case 1—This specimen showed a common atrioventricular canal A common atrioventricular valve extended through the defect, and there was a cleft in the mitral portion of the valve Postmortem examination showed satisfactory repair of the mitral cleft and complete closure of the atrial and ventricular septal defects (Fig 1) Microscopic study showed the atrioventricular bundle lying subendocardially along the posterior inferior margin of the ventricular portion of the atrioventricular canal Suture holes and extensive hemorrhage were observed in the conduction bundle in this area (Figs 2 and 3)

Case 2—This specimen showed the characteristic findings of the tetralogy of Fallot The pulmonary outflow tract had been widened by the insertion of a diamond shaped Ivalon patch which extended into the pulmonary artery The ventricular septal defect (Fig 4) had been incompletely closed, a 4 mm defect persisting in the superior portion Microscopic study showed extensive hemorrhage in and around the conduction bundle (Fig 5), in the area of the posterior inferior margin of the defect (Fig 6)

Case 3—This specimen showed a ventricular septal defect at the origin of the outflow tract of the right ventricle, anterior to the septal leaflet of the tricuspid valve The defect had been closed satisfactorily (Fig 7) Microscopic sections demonstrated suture tracts and hemorrhage in the conduction bundle (Fig 8) along the posterior inferior rim of the defect (Fig 9)

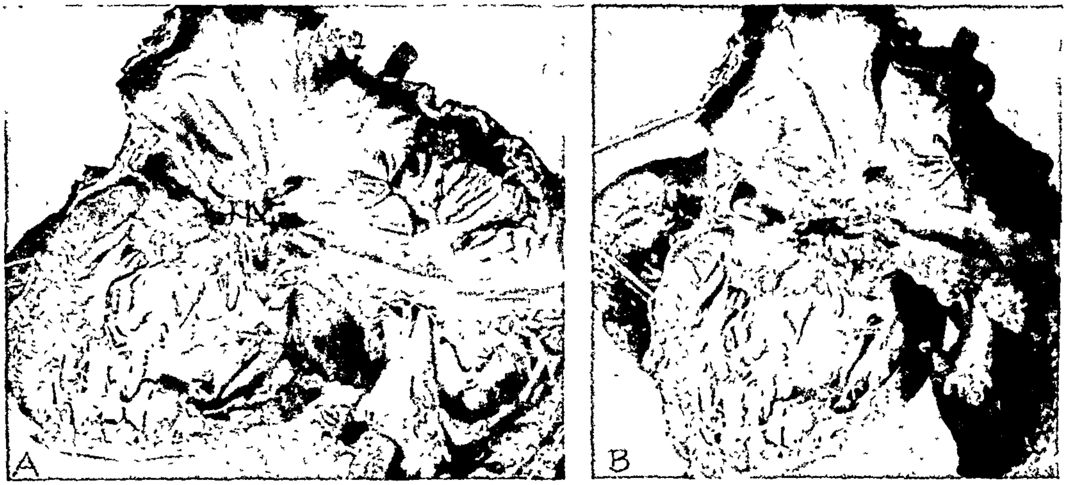

Fig. 1.—Case 1. *A*, Atrioventricular canal, viewed from the right side of the heart. The right atrium lies above and the right ventricle below. The coronary sinus is seen adjacent to the repaired defect. *B*, The sutures have been removed, disclosing the atrioventricular defect.

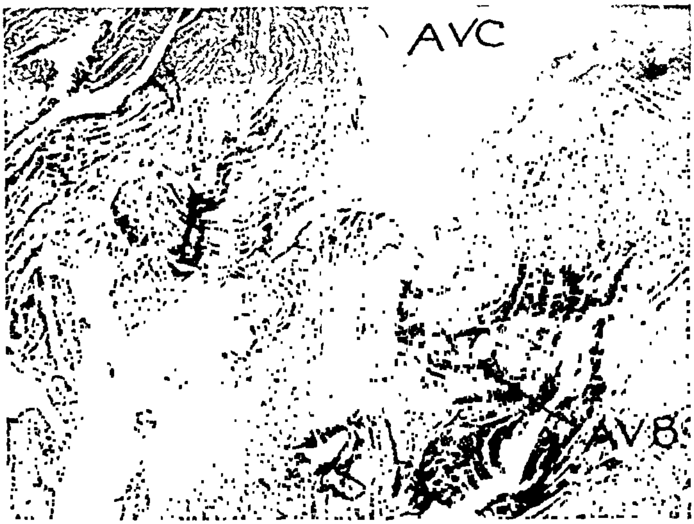

Fig. 2.—Case 1. Photomicrograph showing the atrioventricular canal (*AVC*) and the atrioventricular bundle (*AVB*). Suture holes are seen in the bundle, and extensive hemorrhage is apparent in the area of the conduction tissue.

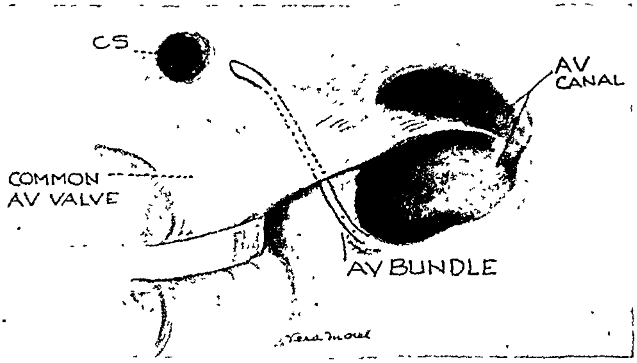

Fig. 3.—Case 1. Drawing of the specimen of atrioventricular canal, showing the relationship of the atrioventricular bundle to the A-V canal. The site of injury of the A-V bundle lay along the posterior-inferior aspect of the defect.

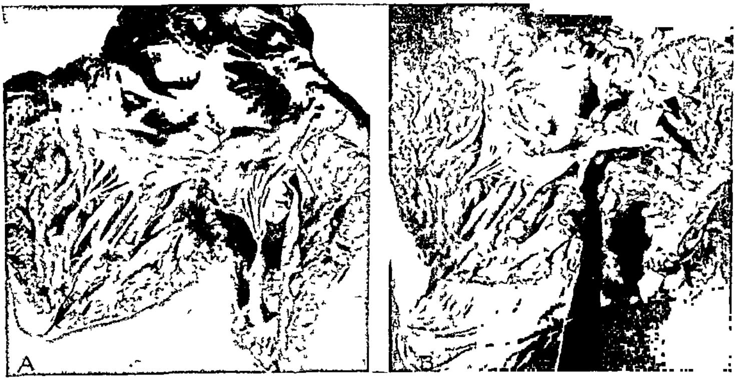

Fig 4.—Case 2 *A*, Tetralogy of Fallot viewed from the right side of the heart Sutures are seen in the ventricular septal defect The outflow tract is not shown *B*, The sutures have been removed and the point of the hemostat shows the location of the ventricular septal defect

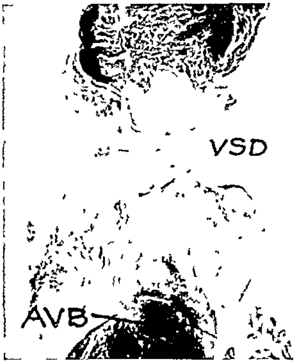

Fig 5.—Case 2 Photomicrograph showing the ventricular septal defect and the atrioventricular bundle There is extensive hemorrhage both in the atrioventricular bundle and in the surrounding ventricular septum

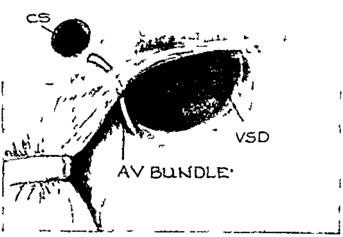

Fig 6.—Case 2 Drawing showing the relationship of the atrioventricular bundle to the ventricular septal defect in the tetralogy of Fallot. The area of hemorrhage occurred along the posterior-inferior aspect of the defect.

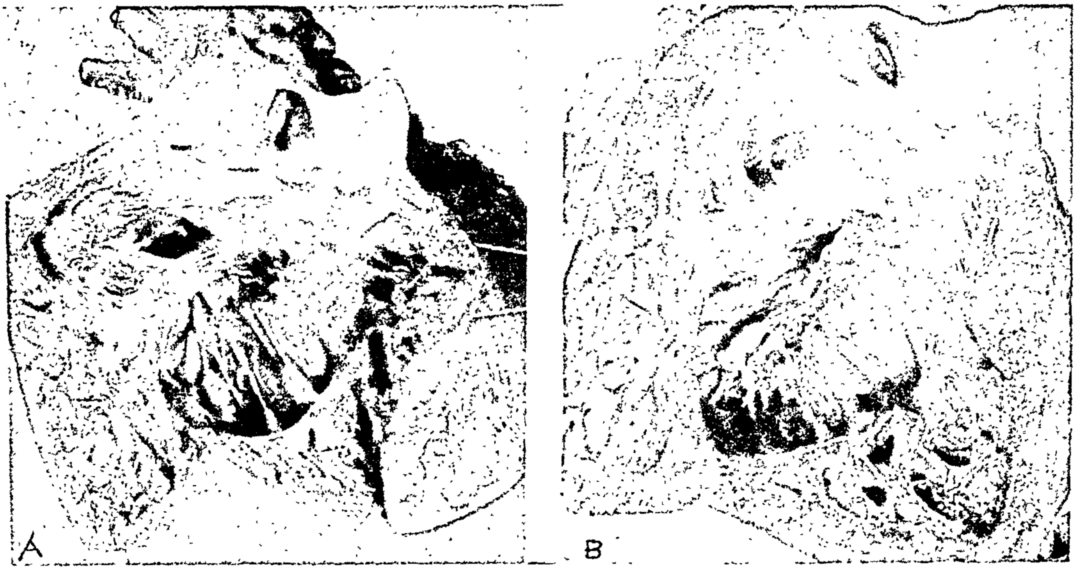

Fig. 7.—Case 3. *A*, Photograph of the case of ventricular septal defect showing the sutures in place. The defect lies at the origin of the outflow tract. The pulmonary valve and artery are seen above the defect. *B*, The sutures have been removed, demonstrating the ventricular septal defect.

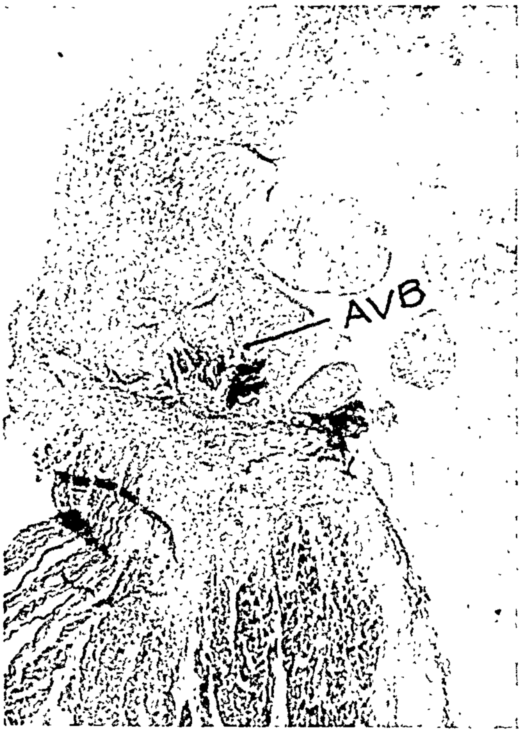

Fig. 8.—Case 3. Photomicrograph showing the atrioventricular bundle above the top of the ventricular septum. A suture tract is seen through the bundle and there is extensive hemorrhage within the bundle itself.

DISCUSSION

The conduction system frequently lies in a vulnerable position in relation to certain intracardiac defects. In the majority of cases of ventricular septal defect occurring as an isolated lesion or in such complexes as tetralogy of Fallot and common atrioventricular canal, the atrioventricular bundle lies subendocardially along the posterior-inferior margin of the ventricular defect.

In the 3 cases included in the present report, heart block occurred following the repair of the cardiac defects in each. In one, the ventricular septal defect occurred as an isolated lesion. In the other 2 cases the ventricular defect was associated with the tetralogy of Fallot in one and with an atrioventricular canal in the other. Yet the site of injury of the conduction system was common to all: the posterior-inferior margin of the septal defect. In each case extensive hemorrhage was noted in and around the bundle in this area, and suture tracts through the bundle were noted in 2.

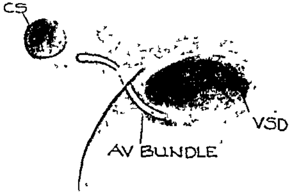

Fig. 9.—Case 3. Drawing of the specimen with a ventricular septal defect The site of injury of the conduction bundle is along the posterior-inferior aspect of the ventricular septal defect

SUMMARY

1. Injuries to the conduction system were studied in 3 cases of complete heart block complicating repair of intracardiac defects.

2. In one case the ventricular septal defect occurred as an isolated lesion. In the other cases the ventricular septal defects were associated with the tetralogy of Fallot in one and with a common atrioventricular canal in another.

3. *Extensive hemorrhage in and around the atrioventricular bundle* occurred in each case. Suture tracts through the bundle were observed in 2.

4. In all cases the site of injury was located along the posterior-inferior rim of the ventricular septal defect.

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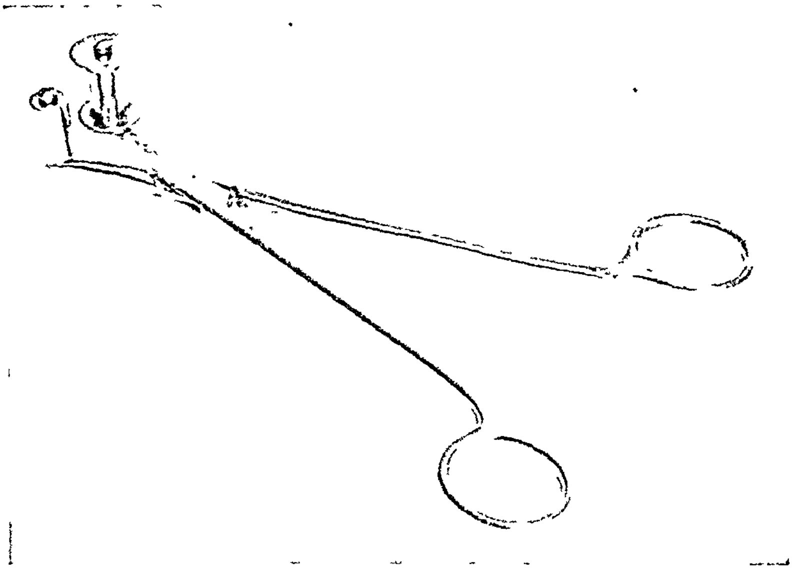
A NEW INSTRUMENT TO MAINTAIN PATENCY OF DRAINAGE TUBES

Gunnar Hey, Copenhagen, Denmark

WHENEVER DRAINS or tubes are used after thoracic surgery, it is important to keep them well functioning and free of pus and blood clots which may be difficult to milk down the tubes.



To facilitate milking down the tubes, we have invented an instrument* with "rolls," as shown in the accompanying figure. It has been used in the Thoracic-Surgical Department at Øresunds Hospital for several months to the great satisfaction of both nurses and doctors.

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*The clamp is manufactured by Simonsen and Weel, Copenhagen, Denmark.

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PRIMARY INTERSTITIAL PULMONARY FIBROSIS: DIFFUSE AND CIRCUMSCRIBED FORMS

Review of the Literature and Report of Eleven Cases

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THE FOLLOWING REPORT on primary interstitial pulmonary fibrosis is presented because of (1) the increasing interest in pulmonary fibrosis, (2) the confusing concepts of its origin and nature, and (3) the gradually evolving idea that a number of separate conditions are, in reality, merely phases of the same disease, so ably presented by Cross.[1] We have summarized some of the pertinent features of the disease in Tables I, II, III. Cases not typical of this disease have been excluded from our series.

HISTORICAL

The credit for recognition of this disease belongs to Hamman and Rich[2] who reported 4 cases in 1935. Pulmonary histologic changes were described in 1931 by Doenecke[3] in a patient who had been in contact with radioactive material. The pathologic abnormalities produced by irradiation[4] are remarkably similar to those of chronic interstitial pulmonary fibrosis. The amount of irradiation received by Doenecke's patient is not known, so it is conceivable that this case was of the primary type and not produced by radioactive material.

Hamman and Rich[5] observed the pulmonary lesions in different stages of development. They believed the disease did not begin simultaneously throughout the lung, but that it spread to involve all lobes. They observed localized

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CASE NO.	AGE, SEX, RACE, AND OCCUPATION	CLINICAL OBSERVATIONS	SIGNIFICANT PULMONARY AND LABORATORY DATA	X-RAY FINDINGS	ESTIMATED DURATION OF DISEASE	SIGNIFICANT PATHOLOGIC FINDINGS
1	75 ♂ white, sawmill planer	Dyspnea, nonproductive cough, chest pain and cyanosis; fine resonant and subcrepitant râles in both bases	Vital capacity, 1,200 c.c.	Widespread diffuse, nodular mottled infiltration throughout both lung fields	15 mo.	Mild fibrous thickening of pulmonary arterioles; vascular hyperplasia; superimposed acute bronchopneumonia
2	63 ♂ white, salesman	Dyspnea, cyanosis, clubbing of fingers and toes and sibilant râles in both lung fields	Vital capacity, 1,150 c.c.; arterial O_2 saturation 72 per cent, after inhalation 100 per cent O_2, 102 per cent	Diffuse reticular pattern of abnormal densities throughout both lung fields	3 yr.	Vascular hyperplasia and mild arteriosclerosis of larger and medium arteries; hypertrophy of right ventricle
3	41 ♂ Negro	Pain in the shoulder			8 mo.	Marked intimal thickening of pulmonary blood vessels; vascular hyperplasia
4	75 ♂ white	Productive cough with blood-tinged sputum and dyspnea; resonant râles throughout both lung fields	Hemoglobin 17.1 Gm.	Shift of the mediastinum to the left and mottled densities in both lung fields	Probably 2 yr.	Slight fibrosis of pulmonary blood vessels, vascular hyperplasia and cor pulmonale; extensive metaplasia and anaplasia of alveolar lining
5	59 ♂ white, mechanic	Dyspnea, productive cough and occasional hemoptysis; dullness in the left base and moist râles in both lung bases	Vital capacity, 1,000 c.c.	Marked mottled densities in the right lung field; left lung field obscured by a calcific plaque	12 mo.	Cirrhosis of lungs; severe vascular hyperplasia of lung parenchyma; extensive metaplasia and anaplasia of the alveolar lining
6	56 ♀ white, waitress	Dry nonproductive cough; clubbing of fingers and musical râles in both lung fields	Decrease of vital capacity from 1,350 c.c. to 750 c.c. in less than one year; arterial O_2 saturation 86 per cent, after inhalation 100 per cent O_2, 106 per cent	Nodular and fibrotic densities throughout the lung fields	10 yr.	Slight fibrosis of wall of blood vessels
7	37 ♀ Negro	Dyspnea, productive cough and chest pain; fine râles over left chest	Vital capacity, 1,300 c.c.; arterial O_2 saturation 91 per cent, after inhalation 100 per cent O_2, 106 per cent	Prominent marking in both lung fields and probable widening of the upper mediastinal region	6 yr. (to date)	Repeated lung biopsy after 21 months of steroid therapy revealed more fibrosis and further increase of anaplasia of the alveolar epithelium
8	39 ♂ white, meat-cutter	Chest pain, slight nonproductive cough, clubbing of fingers, sibilant, sonorous and crepitant râles	Vital capacity, 1,800 c.c.	Diffuse hazy infiltration in both lung fields	4 yr.	Vascular hyperplasia; marked hyperplasia and anaplasia of alveolar lining

forms, and considered localized fibrosis encountered at autopsies to belong to this disease. The great variation in the extent and type of involvement has been emphasized by Cross[1] in his study of 5 cases, and was observed in our cases.

The greater use of lung biopsy has permitted better understanding of the sequence of events from the early stages to almost complete fibrosis of the lung parenchyma. This understanding is extremely important inasmuch as a histologic picture similar to chronic interstitial pulmonary fibrosis may be seen in (1) pneumoconiosis (berylliosis,[6-10] bauxite,[8] asbestosis,[11] etc); (2) collagen disease[12-15]; (3) long-standing chronic passive congestion of the lungs[16, 17] (mitral and aortic stenosis), (4) congenital dysplasia of the lungs[18], (5) pulmonary adenomatosis[19, 20, 21]; (6) sarcoidosis[9, 10, 22, 23]; (7) radiation pneumonitis[1]; (8) histiocytosis[24-27]; (9) obstruction of the pulmonary veins[28]; (10) hypotensive drugs[29, 30], and (11) rheumatoid and rheumatic diseases[16, 31, 32]

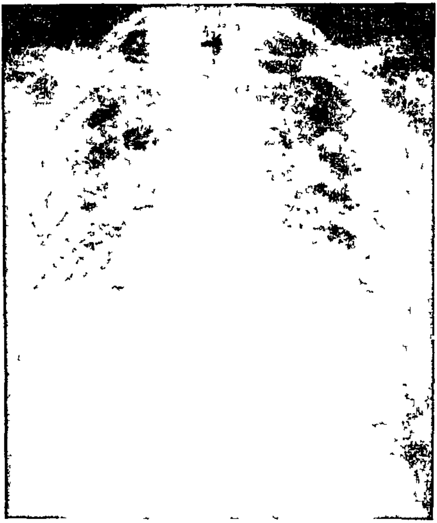


Fig 1 —Case 2 Posteroanterior roentgenogram of chest showing diffuse mottled nodular infiltrations throughout both lung fields, characteristic of diffuse interstitial pulmonary fibrosis

CLINICAL FEATURES

The clinical manifestations of primary interstitial pulmonary fibrosis also vary considerably. The most important symptoms are summarized in Table I. In some patients the prodromal period varies from a few days to several years, characterized by vague general symptoms such as anorexia, weakness, weight loss, easy fatigability, and slight dyspnea. The earliest manifestations are dyspnea, cyanosis, and cough. In addition, there may be fine scattered râles over the lungs and clubbing of the fingers. Slight hemoptysis has been reported, and severe hemoptysis terminating in death in 1 case was recorded by Cross.[1] Chest pain, leukocytosis, or fever have no diagnostic significance. Polycythemia has occurred in several cases, including 1 in our series.

An important factor in diagnostic error is the great discrepancy in roentgenographic findings, subjective symptoms, and paucity of physical findings. The lack of correlation between the subjective symptoms and the physical findings is found in many lesions of the lungs in which a diffuse pathologic process does not impair the transmission of normal sounds.

The roentgenogram may be normal, but more often there are nonspecific reticular and nodular shadows or areas of opacity simulating pneumonic consolidation (Fig. 1). However, these changes may appear in only one lobe or segment.

Rubin and Lubliner[33] have classified cases, according to x-ray appearance, into four groups: (1) patients with minimal abnormal roentgen findings, (2) those with roentgen findings in keeping with cardiac decompensation, (3) patients with roentgen changes compatible with bronchopneumonia, and (4) those with roentgen findings consistent with the changes associated with interstitial fibrosis.

The disease may explode as a rapidly fatal condition or may follow a chronic protracted course. Basically, however, it is a chronic process. The patients reported as having acute disease may have presented an inaccurate history, or may have been seen in the terminal stage. The usual clinical course is one of deterioration of pulmonary reserve. The terminal event is respiratory insufficiency, or right-sided heart failure, or a combination of both.

PATHOGENESIS

Chronic interstitial pulmonary fibrosis occurs most often in young adults, but there is no sex or racial preponderance. In the diffuse form, the youngest patient was 1½ years old and the oldest 75, with an average age of 45. In the circumscribed form, all of the patients were males. The youngest patient was 15 years old and the oldest 60 years, with an average age of 46 years. The etiology of chronic interstitial pulmonary fibrosis is not known. Three of the 4 patients reported by Hamman and Rich[2] had syphilis. However, the relationship to this disease is disproved by the negative serologic test for syphilis in the cases reported subsequently by others.

Viral infections have been considered by some as the most probable etiologic factor. Experimental work by McCordock and Muckenfuss[34] favors the possibility that this type of pulmonary fibrosis may be caused by a virus of mild virulence or present low concentration. Evidence has been advanced against this concept.

Heppleston[35] pointed out that in viral pneumonia the acute interstitial inflammation and the subsequent changes are based upon suppurative bronchiolitis so the lesions are essentially focal and are related anatomically to the bronchioles.

TABLE II SUMMARY OF REPORTED CASES OF DIFFUSE INTERSTITIAL PULMONARY FIBROSIS WITH FAMILIAL PATTERN

CASE NO	AUTHOR AND YEAR	AGE RACE AND OCCUPATION	SIGNIFICANT PULMONARY AND LABORATORY DATA	ESTIMATED DURATION OF DISEASE	SIGNIFICANT PATHOLOGIC FINDINGS
1 (twin sters)	Peabody, Peabody, Hayes, and Hayes[69] 1950	44 white, housewife		3½ yr	Marked intimal thickening of pulmonary arterioles
2	MacMillan[70] 1951	44 white housewife		5 yr	Similar to previous case
3 mother and ughter)	MacMillan[70] 1951	50 white, housewife		Probably 18 yr	Intimal thickening of pulmonary arteries, hypertrophy of right ventricle of heart
4		white		2 yr	Anatomic findings of the lungs similar to previous case
5 isters)	MacMillan[70] 1951	39 white housewife	CO 85 per cent, hemoglobin 18 Gm., RBC 5M, vital capacity 1,100 c c	28 mo	Right ventricular hypertrophy of heart
6		45 white, housewife		3 yr	
7 rothers)	Wildberger and Barclay[71] 1955	52 white bartender		12 mo	Marked intimal and subintimal proliferation of pulmonary blood vessels, hypertrophy of right ventricle of heart
8		38 white, laborer		10 yr	Marked intimal and subintimal proliferation of pulmonary blood vessels
9 isters)	Rubin and Lubliner[33] 1957	58 white		About 3 yr	Thickening of the walls of the medium sized blood vessels
10		40 white		About 4 yr	Moderate thickening of pulmonary blood vessels

TABLE III REPORTED CASES OF CIRCUMSCRIBED PULMONARY FIBROSIS

CASE NO	AUTHOR AND DATE	PATIENT STATUS	EXTENSION OF LESION
1	Cross[1] (1957)	60 ♂	Fibrosis involving the pleura of the left lung and the left lower lobe
2	Cross[1] (1957)	46 ♂	Fibrosis involving the pleura as well as the parenchyma of the right lung
3	Cross[1] (1957)	51 ♂	Fibrosis of pleura and parenchymal tissue of right lower and middle lobe
4	Cross[1] (1957)	15 ♂	Localized mass 7 cm in size in the right lower lobe
5	Cross[1] (1957)	54 ♂	Nodular fibrotic lesions in both upper lobes
6	Baglio, Michel, and Hunter	54 ♂ white	Interstitial fibrosis of the left lung and subsequent involvement of right lung
7	Baglio Michel, and Hunter	45 ♂ white dairy worker	Apical posterior segment of left lung and overlying pleura
8	Baglio Michel, and Hunter	47 ♂ white, laborer	Posterior and superior segments of right lower lobe

Callahan[36] suggested that the disease might be produced by a chronic obstruction of lymph flow since changes in the lung bear a resemblance to spontaneous or experimentally produced lymphedema and elephantiasis. Pokorny[37] and others suggested that the disease may be a sequence of several attacks of interstitial pneumonia with lack of fibrinolytic enzymes and failure of absorption of the inflammatory exudate.

An "allergic" etiology for this condition was suggested by Hamman and Rich.[5] Read[38] described experimental studies in which rabbit anti-rat-lung serum was injected intratracheally in rats. The pulmonary lesions produced in rats had many features similar to the pathologic changes in primary interstitial pulmonary fibrosis.

Many features suggest that the development of this condition is based on an immune mechanism. Eosinophils in the pulmonary lesions are compatible with such an allergic response. The lung lesions in some patients with rheumatoid disease and rheumatic heart disease[31, 32] are identical with interstitial pulmonary fibrosis. Also, there is a morphologic resemblance between the Hamman-Rich disease and such diseases as polyarteritis nodosa,[39] lupus erythematosis, Wegener's granulomatosis,[40] and scleroderma. Even though the etiology of these conditions is obscure, many observers consider them manifestations of tissue hypersensitivity.

The familial tendency (Table II) may reflect a genetically influenced mode of tissue hypersensitivity reaction. The beneficial response of some patients to adrenal steroids is consistent with an immune mechanism.

CASE REPORTS

During the past 3 years we have observed 11 cases of interstitial pulmonary fibrosis of which 8 were the diffuse form and 3 the circumscribed form. In the interest of brevity and for a better comparison with previously reported examples of the diffuse form, our cases of this type have been greatly condensed and will be found in Table I, Cases 1-8, inclusive. Since the circumscribed form has been recognized only recently, we have presented the findings more fully in Case Reports A, B, and C.

In our cases of diffuse involvement (Table I), the diagnosis was made at autopsy in Cases 1 and 2. In Case 3, the diagnosis was established by lung biopsy. The patient died 6 months later and autopsy sections revealed an exacerbation of the inflammatory process in addition to chronic changes. At autopsy, Case 4 was at first considered to have had pulmonary adenomatosis due to the marked hyperplasia and anaplasia of the alveolar epithelium. A more careful review indicated that this was pulmonary fibrosis of the Hamman-Rich type.

Case 5 was diagnosed as having pu[illegible] adenomatosis by lung biopsy and the a[illegible] findings were typical of [illegible] interstitial pulmonary fibrosis. In Case [illegible] is was made by lung [illegible] d a postmortem examination could not [illegible] ed. In Case 7 two [illegible] es were obtained 21 months apart and on different sides. After the first biopsy, the patient was given prednisone 50 mg. initially and then a maintenance dose of 15 mg. daily. The second biopsy showed more fibrosis with an increase of hyperplasia and anaplasia of the alveolar epithelium. In Case 8 the diagnosis was made by lung biopsy and the patient is receiving prednisone. Clinically he is improved, but his vital capacity is progressively deteriorating.

In Case Report A, the left lung biopsy showed the circumscribed form of this disease. Subsequently a diffuse infiltration of the right lung was noted on x-ray examination. In Case Reports B and C, the clinical picture and x-ray studies were suggestive of bronchogenic carcinoma but, on surgical removal of the involved lung, circumscribed interstitial pulmonary fibrosis was found.

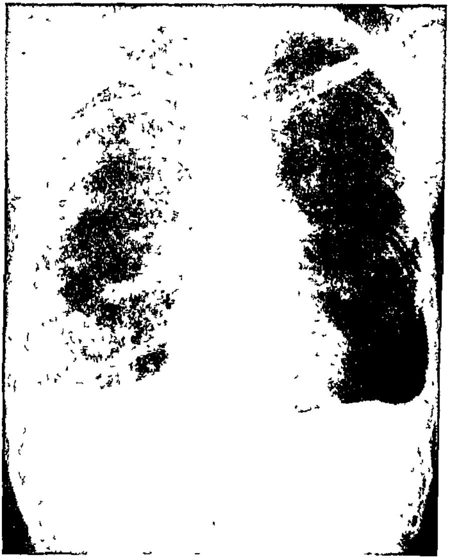


Fig 2—Case Report A. Posteroanterior roentgenogram of chest showing diffuse infiltration bilaterally (more extensive in the right lung) and flattening of the diaphragm, with obliteration of both costophrenic angles

Case Report A.—A 54 year-old white man was admitted to the hospital on Aug. 4, 1956, because of exertional dyspnea and left pleural effusion. He had had rheumatic fever from 1916 to 1918. He was well until 1942 when he noted dyspnea and wheezing which became progressively worse. Positive physical findings consisted of bilateral friction rubs with dullness and crackling resonant râles in the left hemithorax and a diastolic apical murmur. X-ray studies revealed left pleural effusion. Bronchial washing, scalene lymph node biopsy, and biopsy of a granular lesion in the left bronchus were negative. A thoracentesis yielded 300 c.c. of a serosanguineous fluid which was negative for neoplastic cells. Laboratory studies, including skin test for histoplasmosis, coccidioidomycosis, and tuberculosis, were negative. After the thoracentesis, a chest film disclosed marked fibrotic changes in the left lung field and some hazy increased density in the right middle lung field. The patient gave a clinical impression of chronic congestive heart failure due to an old rheumatic mitral valve lesion. A mitral commissurotomy was performed on Sept. 11, 1956. The lung was adherent to the entire parietal pleura, mediastinum, and diaphragm. After operation the patient continued to have a Grade 2-3 diastolic murmur, paroxysmal nocturnal dyspnea, cough, and episodes of dizzy spells.

On May 6, 1959, he was admitted to the hospital complaining of fever of 2 weeks' duration, hemoptysis, and increasing weakness. He was afebrile on admission. A roentgenogram revealed a patchy, diffuse density throughout the right lung with scarring and increased radiolucency in the left lung, flattening of both leaves of the diaphragm, and obliteration of both costophrenic angles (Fig. 2).

A biopsy of the left lung showed a greatly thickened pleura which was smooth and white. Histologically, the pleura had been replaced with thick, vascular collagenous tissue. Some of the alveoli contained a fibrinous exudate, while others were packed with round cells, a great many of which contained brown hemosiderin pigment. Where the wall of the alveoli was well defined, it appeared to be lined by single layers of prominent cells. Occasionally, there was abundant cellular connective tissue which was unevenly distributed within the alveoli. This connective tissue was also abundant between alveoli. The bronchi showed no histopathologic change, but were often found to be embedded in fibrous tissue. The blood vessels of medium size showed only a mild fibrosis of the adventitia with hypertrophy of the intima, but no significant narrowing of the lumen.

In this patient the disease was clinically evident in the left lung and, according to x-ray studies, the right lung was becoming involved. It is possible that both lungs had been involved at the same time but in different degrees.

CASE REPORT B.—The patient, a 54-year-old white truck driver, had worked in a dairy until 1953. For many years, he had had a chronic cough productive of a small amount of sputum which had been attributed to cigarettes. In June, 1958, after spray-painting a car, he developed aching, weakness, feverishness, and increasing cough with expectoration. There was some wheezing but no hemoptysis.

Physical examination at this time was essentially normal except for impaired resonance, bronchovesicular breath tones, diffuse subcrepitant râles, and occasional friction rub over the left upper lobe, contraction and elevation of the left hilum and tracheal shift to the left (Fig. 3). The hemogram and urinalysis were normal. A skin test for tuberculosis was negative. The symptoms subsided following antibiotic treatment, but the chest roentgenogram was unchanged.

On June 30, 1958, at a left thoracotomy, adhesions were found only on the apical portion of the lung. The apical posterior segment was rubbery to palpation and was dissected from the remaining lung. The resected portion of the lung was 16 cm. by 10 cm. by 3 cm. The pleura was thickened and firm yellowish areas were noted near the bronchi and vessels. Histologically the pleura showed dense, vascular fibrous tissue. Alveoli were absent in the dense fibrous tissue areas. In other areas the groups of alveoli were separated by fibrous thickening of the septa. Many of these alveoli were filled with mononuclear cells resembling lipophages, with foamy cytoplasm and a small central nucleus. In some there were a few erythrocytic or phagocytic cells containing pigment. Some alveoli contained fibrinous exudate and a few mononuclear cells. A discrete lymphocytic infiltration was present in some of the fibrous tissue and alveolar septa.

CASE REPORT C.—The patient was a 47-year-old white itinerant laborer who was well until January, 1957, when he experienced sudden right anterior chest pain which radiated laterally and into the right shoulder. One week later, there developed a cough productive of one-fourth cup of yellowish sputum daily and he noticed progressive shortness of breath on mild exertion. At the onset of his illness, he had anorexia and a 20 pound weight loss over a 1-month period preceding his hospitalization on Jan. 30, 1957. He had smoked two packs of cigarettes daily for many years.

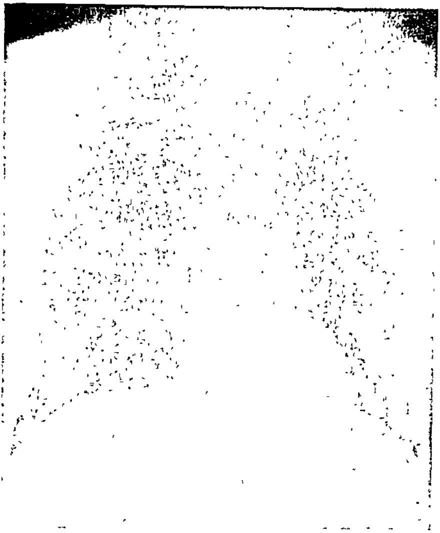


Fig. 3.—Case Report B. Posteroanterior roentgenogram of chest showing mottled and confluent infiltrations of the left upper lung with elevation of the left hilum and shift of the trachea to the left

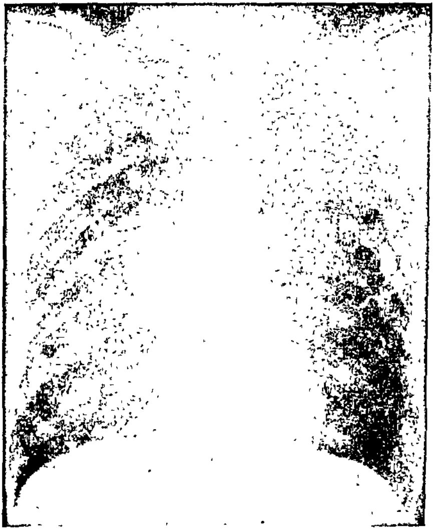


Fig. 4.—Case Report C. Posteroanterior roentgenogram of chest showing enlarged right hilar shadows and parenchymal infiltration of right lung field.

On admission to the hospital, the blood pressure was 115/75 mm. Hg, pulse 96, respirations 30, oral temperature 96.6° F. There was increased AP diameter of the chest with sunken supraclavicular spaces. The chest was hyperresonant to percussion and no râles were heard. Both ankles had 2+ warm pitting edema. Small shotty axillary and inguinal nodes were present bilaterally. The rest of the physical examination was within normal limits.

The red blood cells numbered 3.94 million, hemoglobin was 11.1 grams, white cells 31,250, with a normal differential count; erythrocyte sedimentation rate was 21/100. The sputum studies were negative for acid-fast bacilli.

X-ray studies showed an enlarged right hilum and parenchymal infiltration involving the right lower lung field (Fig. 4). Laminograms demonstrated large masses in the right hilum with compression of the right lower lobe bronchus. Bronchoscopy was normal. Bronchial washings were negative for malignant cells and for acid-fast bacilli on both smear and culture. On March 8, 1957, the posterior and superior segments of the right lower lobe were excised.

The surgically removed lung tissue consisted of two pieces of soft dark-brownish smooth tissue and the entire specimen weighed 180 grams. The pleura was fibrosed and relatively thickened.

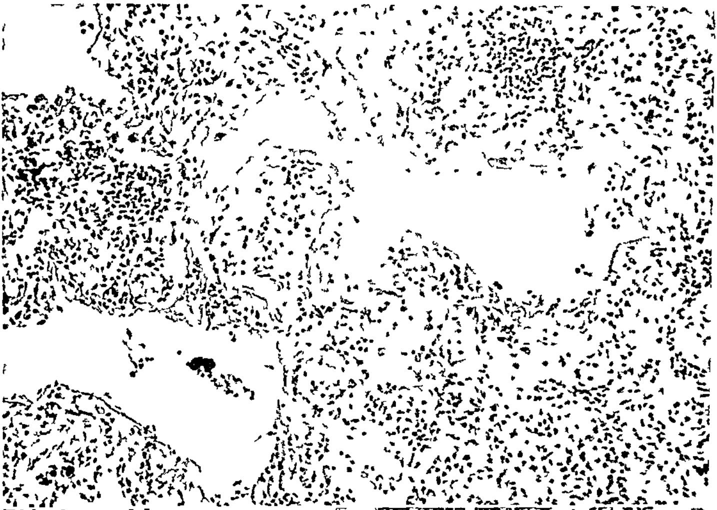
The histologic picture had a striking resemblance to both acute and chronic interstitial pneumonitis. In places where the process was in its active inflammatory phase, there was edema, mononuclear cell infiltration of alveolar walls and albuminous exudate in the alveoli. No hyaline membranes were visible. Older lesions showed vascular hyperplasia, wide alveolar septa, and fibrous encroachment of the alveolar lumina. Focal areas of lung parenchyma had also been completely replaced by fibrous tissue. There were focal collections of lymphocytic cells throughout. Phagocytic cells laden with hemosiderin pigment were present in the alveoli. Small focal hemorrhages were visible in both alveoli and fibrous tissue.

PATHOLOGY

Grossly, the lung is usually solid, and increased in weight and firmness. The pleural cavity may be uninvolved or may show old or recent fibrinous adhesions. The pulmonary lobular markings may be strikingly accentuated on the visceral pleural surface. Small emphysematous blebs can be present. Crepitation is diffusely decreased. The cut surface has a diffuse, web-like fibrotic appearance. In a few instances the lungs have been found to have a marked cirrhotic appearance.

This disease is essentially interstitial and alveolar in location. Both the diffuse and the circumscribed form have similar histologic features. The condition is characterized by an extreme variety of microscopic patterns, including edema, fibrinous exudate, mononuclear cell infiltration of the septa, and focal hemorrhage to the most extreme grade of fibrosis and interstitial collagenous deposition. This variability is probably a result of the following sequence of events: an early stage consisting of fibrinous exudate and predominant mononuclear cell infiltration which involves the alveoli, the septal and interseptal tissue (Fig. 5). This process is followed by an alveolar cell, vascular, and reticulum hyperplasia. The alveolar epithelium undergoes a series of changes from necrosis and formation of hyaline membranes (Fig. 6) in the early phase to regeneration and hyperplasia in the later stages (Fig. 7). There is a striking variation in the number of alveolar blood vessels. There have been cases such as those reported by Golden and Bronk,[53] in which the proliferation of the septal

Fig 5



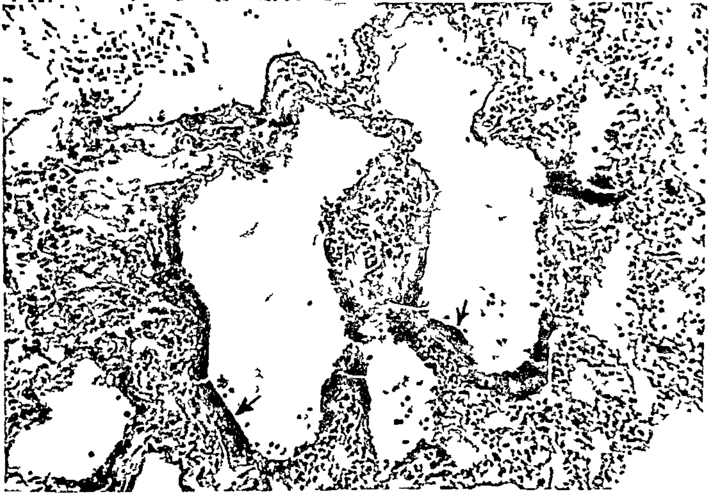
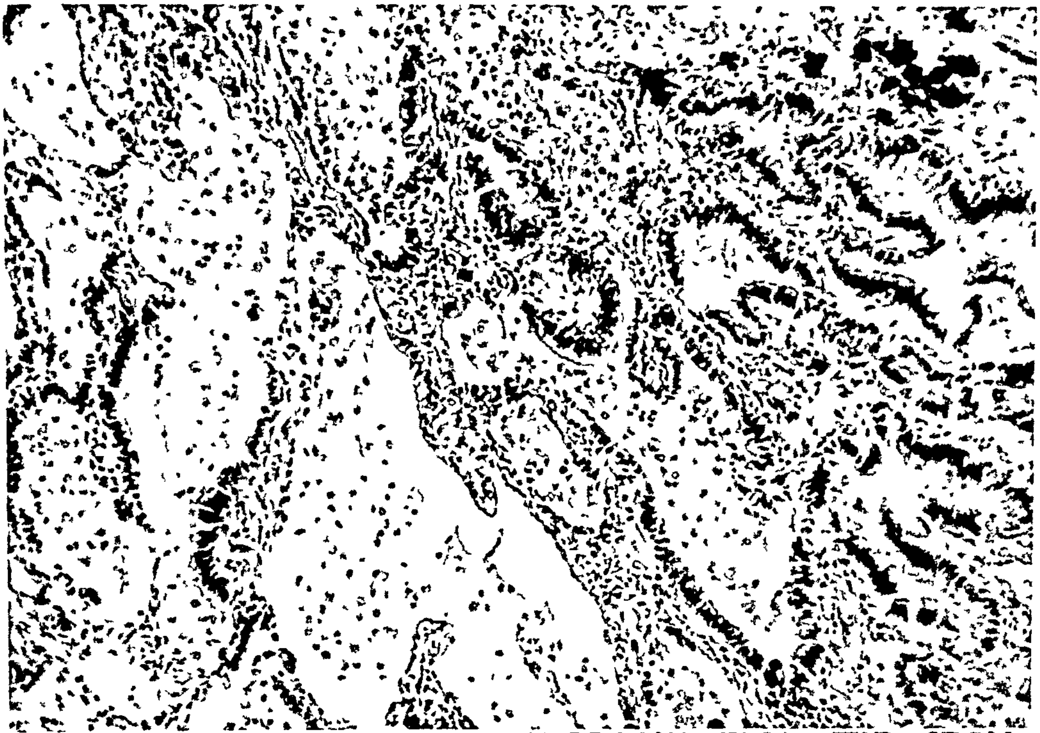


Fig 6

Fig 5 —Case 3 Sections of the autopsy showing exacerbation of the chronic inflammatory process with interstitial and intra alveolar edema, hyaline membranes and necrosis of alveolar walls (×200 reduced ⅓)

Fig 6 —Case 5 Lung section showing hyaline membranes lining the alveoli (×1 0 reduced ¼)

Fig. 7



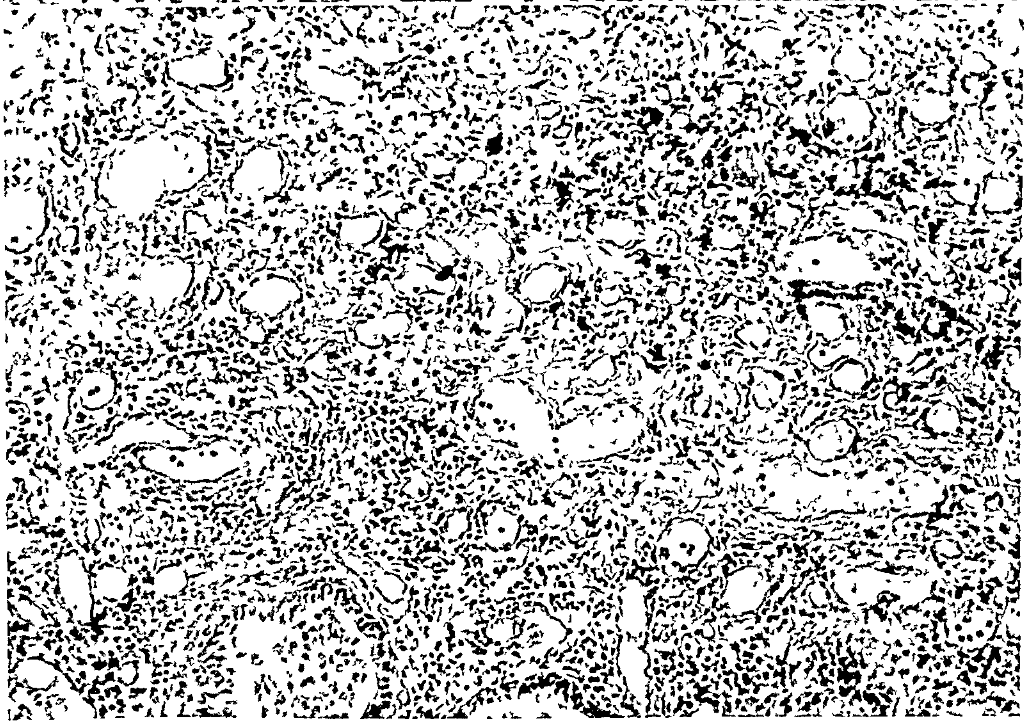
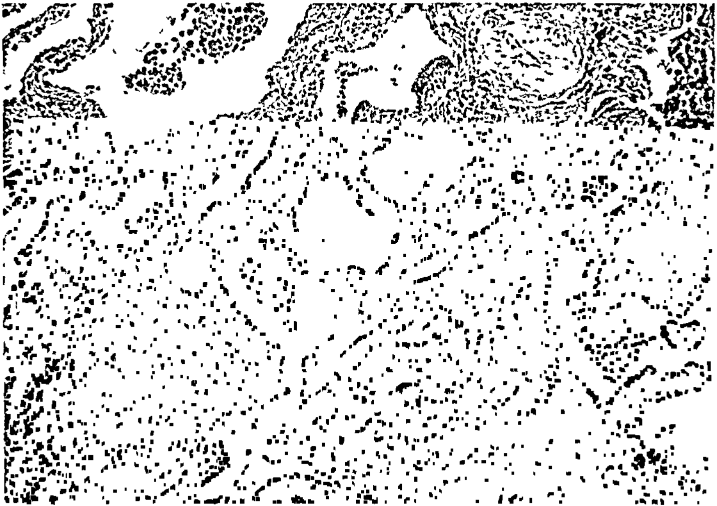


Fig 8.

Fig 7.—Case 5 Lung section showing hyperplasia and anaplasia of the alveolar epithelium with a pseudoglandular pattern, presence of basophilic exudate and mononuclear cells in the alveoli. (×160, reduced ¼)

Fig 8.—Case 5 Lung section showing an area of vascular hyperplasia (×170, reduced ¼)

Fig 9.



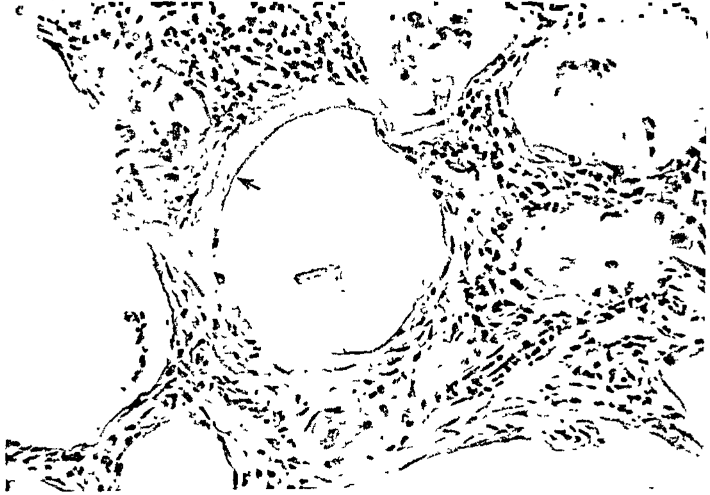


Fig. 10

Fig 9.—Case 3 Lung section of the biopsy showing advanced interstitial fibrosis, chronic inflammation, and intimal thickening of the blood vessels. (×200; reduced ¼.)

Fig 10.—Case 6 Lung section showing organizing hyaline membrane on the surface of the alveolar wall. (×320; reduced ¼.)

capillaries was so striking that the authors called this process "angiosis." The vascular hyperplasia does not have the same significance as the proliferation of blood vessels which occurs in the formation of granulation tissue since, in pulmonary fibrosis, the increased vascularity is usually more striking in areas involved by fibrosis. In all our cases, there have been varying degrees of vascular hyperplasia coincident with fibrosis of the lung parenchyma (Fig. 8).

In the later stages, fibrous tissue begins to proliferate, becoming very cellular and mixed with inflammatory exudate at first, less cellular and rich in collagenous bundles as the process develops (Fig. 9). The fibrous tissue encroaches upon the alveoli leading to a loss of the alveolar pattern and replacement of the alveolar parenchyma with large areas of fibrosis. Shrinkage of the lung parenchyma is brought about in two ways: by organization of the hyaline membranes (Fig. 10) and fibrosis of the interstices and septa, and by encroachment of fibrous tissue upon the alveoli (Fig. 11). When the disease proceeds to the later stages, the patient dies of progressive suffocation. Exacerbation may occur at any time during the course of the disease; this was evident in one of our patients (Case 3, Table I).

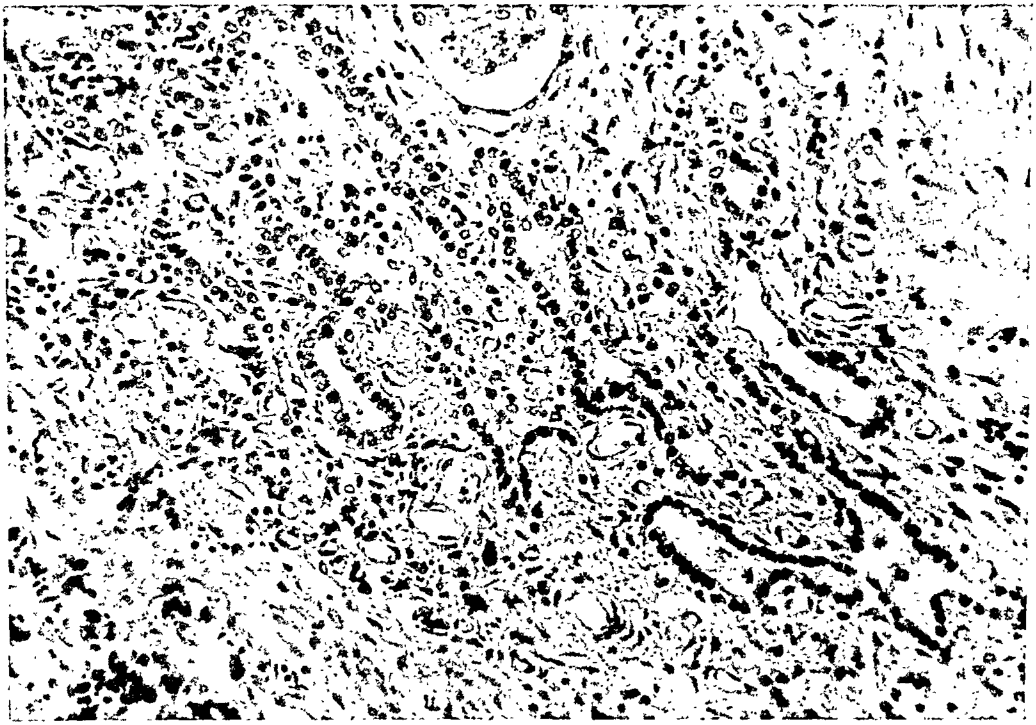


Fig. 11.—Case 5. Lung section showing remnants of alveoli present in the form of cords of hyperplastic alveolar cells buried in fibrous tissue. (×240; reduced ¼.)

The principal changes and the consequent disturbances of pulmonary hemodynamics are caused by septal edema, hyperplasia of capillaries and the reticulum tissue, and by thickening of the septa. These disturbances are comparable to those occurring in cases of long-standing mitral and aortic stenosis.[16, 17] In both conditions, the histopathologic abnormalities of the alveolar septa interfere with the oxygen and carbon dioxide exchange. As pulmonary fibrosis advances, there is impairment in the pulmonary circulation with a gradual rise of pulmonary artery and right ventricular pressure and consequent dilation and hypertrophy of the right ventricle. The pulmonary hypertension is due to the absence of the normal anatomic structure of the alveolar capillaries as well as to the fibrosis, loss of elasticity and intimal thickening of the pre-alveolar arterioles. Of the reported cases of the diffuse form, more than 60 per cent of patients had some degree of cor pulmonale. However, there may be no correlation between cor pulmonale and lesions of the medium and smaller blood vessels.

Differentiation from organized pneumonia can be readily made since chronic interstitial fibrosis has the following microscopic features: (1) the type of inflammation consists of only a few granulocytic leukocytes, mostly mononuclear cells, lymphocytes, plasma cells, and often a small number of eosinophils or

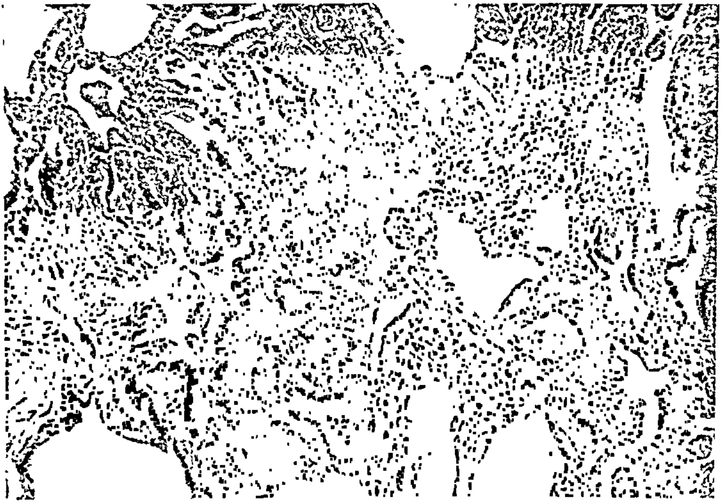


Fig 12.—Case 8 Lung section showing interstitial fibrosis, anaplasia and hyperplasia of the alveolar lining cells in a pseudo-adenoma pattern (×160; reduced ¼.)

occasional giant cells; (2) necrosis of the alveolar walls; (3) fibrinous exudate and hyaline membranes attached to the alveolar walls; (4) marked edema and fibrin deposition in the alveolar walls with consequent thickening of the alveolar septa; (5) hyperplasia, metaplasia, and anaplasia of the lining alveolar cells which often are sloughed off and packed into the alveolar lumina (in many instances they are laden by hemosiderin pigment or have a lipophagic appearance); (6) recent and organizing intra-alveolar and interstitial hemorrhages; (7) absence of any stainable bacteria; and (8) the lesion of the bronchioles consisting of peribronchiolar fibrosis, smooth muscle hyperplasia, some chronic inflammation and squamous metaplasia.

Despite the large number of diseases responsible for pulmonary fibrosis, it is only possible to arrive at a clinical diagnosis when all diagnostic means, including appropriate pulmonary function studies and lung biopsies, are used. The disease which can most closely simulate this condition is pulmonary adenomatosis (Fig. 12). In our series, such an erroneous diagnosis was made twice, once upon study of biopsy material and a second time at autopsy. In one case of Rubin and Lubliner[33] an erroneous diagnosis of metastatic malignancy was made. Transition of pulmonary fibrosis, in any of its forms, into pulmonary adenomatosis[20, 21] is still a subject of dispute, and probably occurs also in the primary interstitial type. The marked alveolar cell hyperplasia and anaplasia (Figs. 7 and 12) characteristic of primary interstitial fibrosis and its close resemblance to adenomatosis can lead to diagnostic error, especially when the study is limited to biopsy material.

PULMONARY FUNCTION STUDIES

The results of vital capacity measurements in our patients with chronic interstitial pulmonary fibrosis are in agreement with those obtained by others. The vital capacity test measures the volume of gas that can be expelled forcefully from the lungs after maximal inspiration. The vital capacity may be reduced by (1) a decrease of lung volume, (2) limitation of chest expansion, (3) limitation to the descent of the diaphragm, and (4) limitation to the expansion of the lungs.

The studies in our patients reveal a diminished vital capacity amounting to one half to one third of normal values. It is reasonable to assume that the major cause of the reduced vital capacity is due to a decreased number of alveoli and to limitation of expansion secondary to fibrosis of large areas of the pulmonary parenchyma. In our patients the rate of air flow during forced expiration was normal as measured by the timed vital capacity. This indicated that even though there was considerable interstitial fibrosis and abnormal alveoli, there was no obstruction to air flow.

Our patients presented evidence of arterial oxygen desaturation since none showed arterial oxygen saturation greater than 95 per cent, the lower limit of normal. After breathing 100 per cent oxygen for 10 minutes, all of the patients brought their arterial saturation from 102 to 105 per cent. A decrease in arterial oxygen saturation may be due to hypoventilation, impairment of diffusion, uneven ventilation related to blood flow, or venous to arterial shunts (intracardiac or intrapulmonary). The venous to arterial shunt is the only mechanism causing arterial oxygen desaturation that is not completely correctable by inhaling 100 per cent oxygen. A venous-to-arterial shunt was ruled out in our patients since the hypoxemia was correctable by 100 per cent oxygen inhalation.

In Case 7, cardiac catheterization showed normal right ventricular and pulmonary artery pressure and normal cardiac output. The pulmonary artery had 71 per cent O_2 saturation and brachial artery 91 per cent O_2 saturation. The ventilation equivalent for O_2 was 3.50 L. per 100 c.c., with the upper limit of normal being 2.50 L. per 100 c.c.

An impairment of alveolar-capillary diffusion for oxygen has been demonstrated in patients having clinical, roentgenographic, and biopsy evidence of pulmonary fibrosis of various etiologies other than Hamman Rich disease[10] Luchsinger and others,[68] in a recent study of 2 cases of primary interstitial pulmonary fibrosis, found an abnormally wide alveolar arterial tension gradient and pulmonary hypertension They concluded that these abnormalities are the result of extensive destruction of pulmonary capillaries These conclusions are supported by a histologic picture of pulmonary vascular hyperplasia, and capillary engorgement, distortion and fibrosis of the capillary blood vessels, loss of elasticity and intimal thickening of the pre alveolar arterioles

THERAPY

Before 1952, the treatment of chronic interstitial pulmonary fibrosis was usually symptomatic, consisting of expectorants and antitussive agents In 1952, adrenal steroids were introduced along with the increased use of lung biopsy as a diagnostic measure

Of the 23 patients previously reported who have been treated with steroids, only 3 showed any remarkable clinical improvement with the total disappearance of symptoms and clearing of the chest roentgenograms[51 54 59] Of these cases, two of the patients died a few days after discontinuing steroid therapy,[51 54] while the third patient is still alive and asymptomatic after 8 months of continuing administration of cortisone[59] Ten patients had no clinical improvement[33 36 48 50 51 58] In 9 other cases, there was some temporary improvement,[33 50 54 66 67 68 71] but without change in the course of the disease In 3 of these last 10 cases, there was an exacerbation of symptoms and death following the reduction or withdrawal of steroid therapy[54 71] White and Craighead[69] reported a patient who had exacerbation of symptoms following cessation of steroids with prompt response to restitution of therapy

Three of our patients who received steroids had no symptomatic improvement, and, in one of them, the vital capacity has progressively deteriorated A fourth patient has been receiving steroids for a period of 3½ years with symptomatic improvement of dyspnea, even though there has been steady reduction of the vital capacity

The rationale for the use of adrenal steroids is based upon its anti-inflammatory and anti exudative effect[70] Beneficial effects have been reported in those patients in whom the disease process was in a relatively early stage Once fibrosis becomes established, it appears to be irreversible and the patients receive only temporary benefit

Hamman and Rich considered this disease to be due to a hypersensitivity reaction Steroid therapy would be indicated if the main pathologic features of this disease were due to an established allergic tissue reaction Steroids probably do not alter the stimulating factors but simply alter the tissue response of the host

In 5 patients, there was an exacerbation of symptoms and death following the cessation or the decrease of steroid dosage, while another patient responded to restitution of steroids. Because of these disastrous results,[73] many investigators feel that once steroid therapy is instituted, it must be continued indefinitely.

To realize the full beneficial effects of adrenal steroid therapy, it is imperative to make the diagnosis early. Since clinical manifestations are so varied, it is worth while to resort to lung biopsy more often for early diagnosis.

SUMMARY

The pertinent features of 77 cases from the literature and 11 cases of our own series of primary interstitial pulmonary fibrosis of both the diffuse and the circumscribed type have been presented and analyzed. The etiology is unknown.

The earliest clinical manifestations of this disease are dyspnea, cyanosis, and cough. In addition, there may be clubbing of fingers, râles, weakness, and weight loss. There is a high incidence of arterial oxygen desaturation and decreased vital capacity. X-ray studies are not diagnostic but usually show nonspecific reticular densities bilaterally.

Histologically, one sees intra-alveolar exudate and cellular infiltration. The changes in the alveolar wall include necrosis, regeneration, hyperplasia, anaplasia, and fibrosis. The demonstrable changes in the blood vessels consist of hyperplasia, fibrosis, and intimal thickening. Because of these changes, the mode of death usually is either pulmonary insufficiency or right heart failure, or both.

Diagnosis of this disease is often made by lung biopsy. There is no "typical" histologic picture and this disease can be easily confused with pulmonary adenomatosis and other conditions.

It appears from previously reported cases and from our own series that the current treatment of choice is adrenal steroids, even though the effect in many cases has been negligible. Because of the risk of precipitate death following the discontinuance of steroids, it is necessary to continue such therapy indefinitely once it is undertaken.

The authors wish to thank Dr. John E. Tuhy, Portland, Oregon, for permitting us to include 2 of his cases in this study.

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AN INQUIRY INTO THE CAUSES AND PREVENTION OF COMPLICATIONS IN RESECTION SURGERY FOR PULMONARY TUBERCULOSIS

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THIS STUDY comprises an analysis of the resections for pulmonary tuberculosis done on the Thoracic Surgery Service of Highland-Alameda County Hospital, Oakland, California, during the period January, 1946, through and including December, 1956. There were 288 resections in 274 patients. All cases were histologically proved to be tuberculous; a bacteriologic diagnosis was made on the majority of them. These patients have been followed from 1 to 11 years. They were all covered by antituberculosis drugs as the drugs became available, although a few of the earlier patients had either no antimicrobials or only short 60-day courses of streptomycin. Para-aminosalicylic acid (PAS) and isonicotinic acid hydrazide (INH) have been added in the usual dosage and for the length of time employed in most clinics. In a few cases of an undiagnosed pulmonary lesion, patients were operated upon without adequate preoperative antimicrobial preparation, but drugs were administered in these patients when tuberculous pulmonary tissue was resected. Almost all the patients in the later group had the usual 6 to 9 months sanatorium care including drugs, and many of them had pneumoperitoneum as well. The indications were the usual ones and the earlier series includes many cases of late bronchostenosis of the main-stem bronchus, destroyed lung, uncontrolled cavity, tension cavity, and thoracoplasty failure. Because of the absence of, or short courses of chemotherapy in the earlier cases, and because of the difference in the types of tuberculosis in the patients coming to operation in the earlier years compared with the types of disease treated later, the series has been arbitrarily divided into two 5½ year periods, the first from January, 1946, through June, 1951, and the second from July, 1951, through December, 1956. The same surgical technique was used in all of the resections. Fewer resections were done in the earlier years of the series (72 resections) than in the last 5½ years (216 resections). In the first 5½ years there were 20 resections with complications (27.8 per cent) and in the latter half there were 41 complications (19.0 per cent). The over-all complication rate was 23.8 per cent. The mortality rates for the two periods were approximately equal:

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11 2 per cent in the first 5½ years, 9 8 per cent in the second group, and the over all mortality rate was 10 6 per cent (29 deaths in 274 patients) Some patients had multiple complications, there were 69 major complications in all Five patients in the group with complications had 2 resections during the period of study, and 7 patients in the group with no complications had 2 resections All of the patients were operated upon under fairly standard conditions, including good anesthetic supervision by a physician anesthetist Blood transfusions were available throughout the series, and there was only one transfusion reaction resulting in a fatality During the 11 year span there have been improvements in surgical technique, learned by the experience of all concerned The techniques and agents used in anesthesia have also improved In addition to the advent of antituberculosis drugs there has been better management of pyogenic infections with the newer broad spectrum antimicrobials Pyrazinoic acid amide (pyrazinamide) and viomycin were used in some of the drug resistant cases in the later group

OPERATIVE TREATMENT

Fifty three patients underwent pneumonectomy, 125 lobectomy, 31 patients had removal of a lobe plus a segment, 74 had segmental resection, and there were only 5 wedge resections In the pneumonectomies performed, there were complications in 15 cases, and there were 9 deaths directly or indirectly the result of surgery Twenty seven patients having lobectomies developed complications and 8 of these died In the patients who had resection of more than a lobe but who had less than a pneumonectomy, there were 7 complications with 4 deaths Twelve patients subjected to segmental resections had complications, 8 of whom died There were no complications in patients having wedge resections With regard to space diminishing procedures, there were 21 thoracoplasties performed (either pre resection or concomitant or both) in the group with complications and 71 in the other group, a total of 92 The 6 thoracoplasties (pre resection or concomitant) done in the 74 segmental resections were performed in connection with some previous operation or as a modified thoracoplasty These 6 are not analyzed There were approximately 30 per cent thoracoplasties in all three categories total operations, patients developing complications, and those not having complications Therefore, no statistical significance is attached to them However, the space diminishing procedures done for certain key complications which the author believes are important with relation to thoracoplasty, are broken down as follows of the 14 patients with bronchopleural fistulas, only 4 had concomitant thoracoplasty, of the 7 with empyema, 5 had thoracoplasty (pre resection or concomitant), two thirds of the patients with tuberculous spreads, one fourth with ventilatory insufficiency, and one sixth of those developing atelectasis had space diminishing procedures

ANALYSIS OF THE COMPLICATIONS

A broad summary of the complications can be seen in Table I, which shows their incidence and the number of deaths with each type of major complication The most commonly occurring difficulty was bronchopleural fistula with or

TABLE I. COMPLICATIONS

	NUMBER		DEAD	
Bronchopleural fistula				3
a. With empyema		8		
b. Without empyema		6		
Empyema		7		1
Pulmonary edema		9		7
Hemorrhage		7		3
Shock		6		6
Ventilatory insufficiency		4		2
Acute spread of tuberculosis		3		0
Wound sepsis		4		0
Atelectasis		6		3
Miscellaneous		9		5
Lower nephron nephrosis	2		2	
Paradoxical chest wall leading to poor drainage and requiring further surgery	1		0	
Stump abscess with reactivation TBC in bronchiectatic divisional stumps	1		–	
Severe reaction to local anesthetic	1		1	
Subcutaneous emphysema requiring tracheostomy	1		–	
Cardiac standstill	3		2	
Totals		69		29

without empyema. Pulmonary edema (or cor pulmonale or right heart failure) occurred 9 times with 7 deaths. Empyema, hemorrhage, shock, atelectasis, ventilatory insufficiency, wound sepsis, and acute spread of tuberculosis occurred in that order of frequency. There was a miscellaneous group of patients accounting for 9 major complications, 5 of whom died. Seventy-nine per cent of the patients developing complications had positive sputum, whereas 68 per cent of the group without complications were sputum positive. These complications are further analyzed in tabular form.

The "tuberculous complications" occurred much more frequently in patients with positive sputum: 11 out of 14 with bronchopleural fistulas (Table II), all of those with empyema (Table III), and all of those with tuberculosis spread (Table IV). Fistula occurred more frequently following lobectomy than in any other type of resection. In 2 cases, a segment was removed in addition to a lobe. There was only one bronchopleural fistula which followed pneumonectomy, and this occurred in a patient who had not had concomitant thoracoplasty. There were 5 cases of bronchopleural fistula in which the bronchoscopic note mentioned a "red" bronchus. There were 3 additional cases in which either no bronchoscopy was done or the bronchoscopy was performed many weeks before the resection. The one case (No. 29) of mass ligature of the bronchovascular pedicle, done to control hemorrhage, was followed by a bronchopleural fistula. The patient who developed a fistula following pneumonectomy for destroyed lung had bronchoscopic evidence of extensive tracheobronchial disease, with stenosis of the main-stem bronchus. This patient (No. 6) had uncontrolled positive sputum and, in desperation, steroids were given preoperatively in an effort to control the tracheobronchitis. The cavity was entered at surgery and, following pneumonectomy, a fistula developed on the tenth day; the patient died on the thirteenth day. That was the one and only instance of ACTH being administered to a tuberculous subject on this service.

From Table II it can be seen that inadequate drug coverage, particularly in the early part of the series, may have been partly responsible for the fistulas. In analyzing these 14 fistulas there is only 1 case (No. 5) in which there is no apparent cause. This was an instance of a destroyed right upper lobe and a large cavity in the right lower lobe in which a lobectomy plus segmental resection was performed in the presence of a quiescent bronchus and with adequate drug coverage. Concomitant thoracoplasty was done; yet multiple fistulas occurred, which required three operations. There was a final good result.

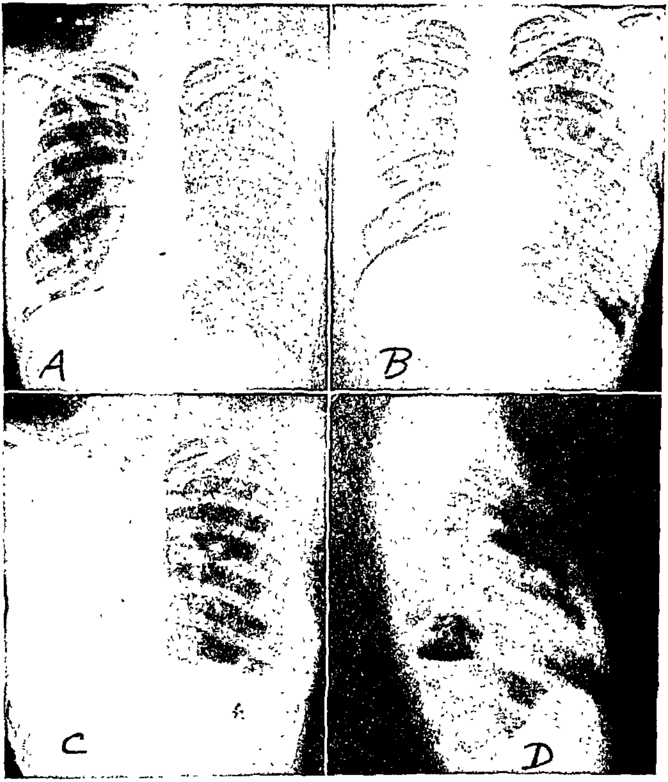

Fig. 1.—Case 10. *A*, Atelectasis, right middle and right lower lobes, due to bronchostenosis.
B, Following bilobectomy (right middle and right lower lobes).
C and *D*, Two and one-half years later, bronchopleural fistula and spread on right side. Empyema was drained with Eloesser flap, but patient died 6 months after fistula appeared.

TABLE II.

NO.	AGE	SPUTUM AND SENSITIVITIES	PREOPERATIVE BRONCHOSCOPY	DRUGS COVERING SURGERY	TYPE OF DISEASE
3	26	pos.	RLL, RML red and stenotic—2 mon.	SM, PAS	Destroyed RML, RLL
5	37	pos.	Quiescent	SM, PAS, INH	Destroyed RUL; large cavity RLL
6D	23	pos.	Extensive tracheobronchial disease with RMB stenosis	SM, PAS, INH	Destroyed lung; tracheal stenosis and giant cavity
10D (Fig. 1)	26	pos. (resistant to SM)	Red, narrow RML and RLL	PAS	Atelectatic RML, RLL; tracheobronchial disease
14	45	neg.	No endobronchial disease, but endoscopy 6 wk. prior to surgery	SM, PAS, INH	Cavity RUL and superior segment of RLL
16	45	pos.	"OK for resection"	SM, PAS, INH	Cavity A-P segment LUL
26D	31	pos. (slightly resistant to SM)	Red, friable mucosa at LMB, LLL	PAS	Giant tension cavity, LUL
29	32	neg.	No stenosis or edema	—	Tbc. bronchiectasis, LLL
31	53	pos.	Not done	SM	Chronic abscess LUL; Eloesser flap drainage
44	28	neg.	Normal	SM, PAS, INH	Cavity, RUL
45*	42	pos.	LMB slightly reddened	SM, PAS	Cavity, LUL
45	47	pos. (resistant to all drugs)	Chronic striations; no acute inflammation	INH added to regimen	Cavity, LLL and apex of chest
46	35	pos.	Not done	SM, PAS	Cavity, LUL
50	25	pos. (resistant to PAS, SM)	Normal	SM, PAS, and viomycin	Giant cavity RUL and fibrocavitary Tbc, RML, RLL

*The same patient had separate fistulas with the 2 resections.

Studies on the resistance of the tubercle bacillus to various antimicrobials were not done on all of the patients in this series. Twenty-one patients with positive sputum in the group which developed complications had resistance studies. It is interesting to note that of the tuberculous complications there were 7 resistant cases: 4 of the 11 patients in the group which developed fistulas

BRONCHOPLEURAL FISTULA TABLE

THORACOPLASTY	OPERATION	WITH EMPYEMA	RESULTS	CAUSE
No	Bilobectomy (RML, RLL)	Yes	Fistula, 14th day, requiring 4 operations to close, *died* of pulmonary edema	Bronchus was red, preop
Yes, concomitant	Lobectomy plus segmental resect	Yes	Multiple fistulas, requiring 3 operations final result good	No cause apparent from chart analysis
No	Pneumonectomy	Yes	Fistula 10th day, *died* 13th day	Steroids given preoperatively, cavity entered at surgery
No	Bilobectomy (RML, RLL)	No	Fistula 3 years later RLL stump *died*	Bronchus was red, preop
No	Segmental resect	Yes	Fistula after 1 mo requiring 2nd operation, good result	No immediate preop bronchoscopy
No	Segmental resect	No	Fistula after 10 mo requiring thoracoplasty good result	Emphysematous lungs
No	Lobectomy	Yes	Fistula 11th day, *died*	Bronchus was red, preop
Yes, concomitant	Lobectomy	No	Fistula 3rd week controlled by bronchoscopic $AgNO_3$ cauterizations	Mass ligature bronchovascular pedicle to control hemorrhage
No	Lobectomy and excision Eloesser flap	Yes	Fistula continued after drainage tubes removed, two further operations, good result	Drug coverage not good, as Tbc was not suspected
No	Lobectomy	No	Air leak continued requiring thoracoplasty on 12th day	Bronchoscopy 1 mo pre op, emphysema
No	Lobectomy	Yes	Fistula 1st day requiring multiple operations including a 2nd resection (see below)	Bronchus red at endoscopy 2 months preop, LMB inadvertently entered at surgery
Yes, preresect and concomitant	Segmental resect	Yes	Fistula 3rd week requiring multiple operations, spread to right, *died*	Uncontrolled positive sputum
Yes concomitant	Lobectomy	Yes	Fistula treated by pneumonectomy, *died* 3rd day postop pneumonectomy	No bronchoscopy prior to 1st resection
No	Lobectomy and segmental resect	No	Fistula 1st week, requiring 2 operations, poor result with basal empyema	Should have had preresection or concomitant thoracoplasty

had resistance to one or more drugs, 1 out of 7 of the patients with empyema had resistance to three drugs, and 2 of the 3 patients with acute spread were resistant to one or more drugs

Table III shows that in all 7 of the cases of empyema there had been positive sputum, and in 5 of them there had been inadequate drug coverage as

TABLE III. EMPYEMA

NO.	AGE	SPUTUM AND SENSITIVITY	*DRUGS* COVERING SURGERY	TYPE OF DISEASE	THORACOPLASTY	OPERATION	RESULTS	CAUSE
11	30	+	PAS	Bronchostenosis	Yes, concomitant	Pneumonectomy	Good following rib resection, drainage	Insufficient drug coverage
13	37	+	—	Destroyed cavitary lung	Yes, concomitant	Pneumonectomy	Required 2 more thoracoplasties and en bloc excision of *empyema*	Cavity ruptured at surgery soiling pleura; no drug coverage
15	42	+	SM, PAS, INH	Contracted, destroyed RUL	No	Lobectomy	Fluid-air collectia didn't respond to tubes, irrigation, etc., required thoracoplasty	—
20	43	+ Resistant to SM, PAS, INH	SM, viomycin	Fibrocaseous, cavitary upper lobe and empyema	Yes, preresection	Pneumonectomy	Wound dehiscence 9th day; empyema required total thoracoplasty in 2 stages	Pleura contaminated at surgery; patient malnourished
25	53	+	—	The bronchiectasis LUL un*der thoracoplasty*	Yes, preresection	Lobectomy	Large fluid-air level 10th day, draining through wound dehiscence; *died* 21st day	No drug coverage
36	22	+	—	Cavernous LLL	No	Lobectomy	Large pleural space 6th day, empyema 12th day, healed with drainage	Last bronchoscopy 5 mo. preop.; no drug coverage
41	50	+	PAS	Destroyed lung	Yes, concomitant	Pneumonectomy	Empyema 3rd week; improved following two more operations	Pleura contaminated at surgery; insufficient drug coverage

judged by our present day criteria. All of the instances of empyema followed either lobectomy or pneumonectomy, and there were only 2 patients who did not have thoracoplasty, either pre resection or concomitant. In addition to no drug coverage or insufficient drug coverage for the cases of empyema, there were 3 cases of soiling of the pleura by cavity contents. In 1 such patient (No 20), with resistant organisms, pneumonectomy was done under a (pre resection) thoracoplasty for a destroyed lung. This empyema was further complicated by wound dehiscence, which required completion of the thoracoplasty in two stages, followed by an eventual good result.

Acute spread of tuberculosis following surgery is tabulated in Table IV, showing that no drug coverage or inadequate drug coverage was a factor in 2 patients, and, in the third, in whom three drugs were given, studies had shown total resistance. Two of the 3 patients also had a "red" bronchus.

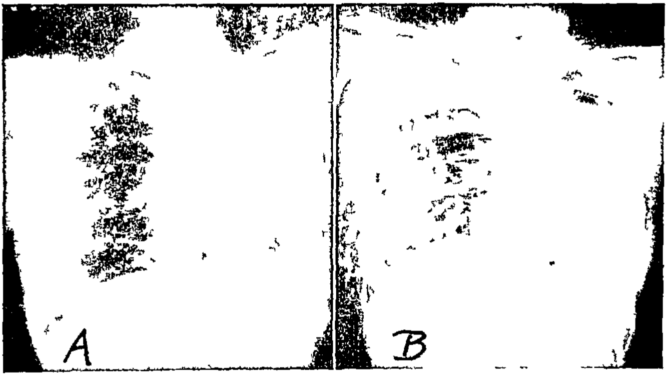

Fig 2.—Case 24. *A*, Atelectasis cavitation left lung with tracheobronchial disease. *B*, Spread to right side 17 days following pneumonectomy. Patient died 2 years later.

The complication of acute pulmonary edema occurred most commonly following pneumonectomy as would be expected. Pulmonary edema and ventilatory insufficiency are tabulated together (Table V). Four of the patients with ventilatory insufficiency should have had early tracheostomy and perhaps tracheostomy with prolonged artificial respiration, as many of them had retained secretions and underwent numerous bedside bronchoscopies. Hemorrhage in surgery, extensive and difficult operations, advanced age, emphysema, etc, all played a part in the development of pulmonary edema in these patients as can be seen from the last column in Table V.

The complication of severe hemorrhage is tabulated together with shock, (Table VI). The latter is a classification under which 6 cases are tabulated after exhaustive analysis of the records failed to reveal any better cause for the complication. All 6 patients in shock died. Of the 7 cases of hemorrhage, 3 patients died in the immediate postoperative period or within the first 2 weeks,

TABLE IV. ACUTE OPERATIVE SPREAD OF TUBERCULOSIS

NO.	SPUTUM SENSITIVITY	PREOP. BRONCHOSCOPY	DRUGS	TYPE OF DISEASE	OPERATION	EXTENT REMAINING DISEASE	POSTOP. BRONCHOSCOPY	CAUSE
21	pos.	Red bronchus	—	Giant RUL cavity (bilateral disease)	Lobectomy (RUL, RML) concomitant thoracoplasty	Extensive fibronodular Tbc, RLL	Yes	No drug cover, bronchus red, pleura soiled at surgery
24	pos. (resistant to SM)	Redness, LMB and laryngeal tubercles	Tuberculin (Fig. 2)	Destroyed lung and tracheobronchial disease	Pneumonectomy	—	Yes	No drug cover, bronchus red
45	pos. (totally resistant)	No acute inflammation	SM, PAS, INH	Cavity LLL and apex of chest under thoracoplasty (post LUL chest)	Segmental resect.; revision thoracoplasty	BP fistula present apex of chest	Yes	Organism drug-resistant Tbc transect. at surgery

3 had re exploration and removal of the clotted blood or decortication, and 1 was improved following conservative treatment (Figs 3 and 4) In this group of 13 cases of shock and hemorrhage there is no discernible cause for the development of the complication in 3 However, in the other 10 cases mention was made of difficulty with hemostasis at surgery, or some factor is brought out in the clinical summary of the case which gives a hint as to why it occurred

Table VII shows the 6 cases of serious atelectasis and attempts to analyze their causes All of these patients had immediate postoperative bronchoscopies Two of them (No 12 and No 55) would have benefited from early tracheostomy, in retrospect, and 1 patient (No 39) received a large dose of morphine on the first night which may have depressed the respirations The patient was a 58 year old man who had undergone lobectomy for a mass thought to be a carcinoma The lesion was tuberculous, and he had repeated episodes of atelectasis which required bronchoscopy at the bedside

There were 4 cases of wound sepsis This complication occurred following pneumonectomy in a rather poorly nourished man (No 20) who had a history of alcoholism His course was further complicated by the development of an empyema, treated by total thoracoplasty in two stages with a final good result (referred to above) Another wound sepsis occurred in a patient (No 21) who underwent a bilobectomy for giant cavity, and whose course was complicated by acute spread which cleared with bronchoscopy This individual developed a nonspecific granulomatous infection of the sternomanubrial joint and the sternum which required four operative procedures on the chest wall with a good result This patient had had contamination of the pleura during surgery Another patient (No 25) had a lobectomy for tuberculous bronchiectasis under a thoracoplasty This patient died soon after operation with a combination of wound dehiscence and empyema No obvious cause for this catastrophe could be found except that there had been no antituberculous drug coverage The final case of wound sepsis (No 49) occurred in a middle aged diabetic woman undergoing lobectomy for a right upper lobe cavity in the presence of bilateral disease She developed chest wall abscess some weeks after operation which required two operative procedures to débride and marsupialize the infected chest wall Wound infection has been reported in fairly high incidence in cases in which pulmonary resection for tuberculosis has been done This has not been our experience, although in recent years there has been a definite increase in superficial wound sepsis due to the ubiquitous staphylococcus

The remaining serious complications are classified under a miscellaneous group in which there were 2 cases of lower nephron nephrosis, 1 case of paradoxical movement of chest wall, 1 stump abscess with reactivation tuberculosis in bronchiectatic lobar divisional stumps, 1 severe reaction to a local anesthetic, 1 case of subcutaneous emphysema requiring tracheostomy, and 3 cases of cardiac standstill The cases in the miscellaneous group have little in common and are not tabulated One of the cases of lower nephron nephrosis was due to a transfusion reaction The case of severe paradoxical respiration was due to an unstable chest wall probably due to the use of formalin in a previously done thoracoplasty This individual had difficulty raising secretions after the

TABLE V. PULMONARY EDEMA AND V[illegible]RY INSUFFICIENCY

NO.	AGE	OTHER ILLNESS	TYPE OF DISEASE	OPERATIONS	RESULT	COMMENT
3	26	Long-standing suppuration	2 BP fistulas	Lobectomy and concomitant thoracoplasty	*Died* on 4th day of pulmonary edema	Poor general condition
4	36	Enlarged liver	Destroyed lung, BP fistula	Pneumonectomy	Heart failure and *death,* 4th week	Hemorrhage in surgery
18	74	Chronic asthma, emphysema	Undiagnosed lesion, RLL	Segmental resect.	*Died* of pulmonary edema 10th day	Advanced age; emphysema; no drug coverage
19	39	Laryngeal disease, Pott's disease earlier	Destroyed lung	Pneumonectomy	*Died* in O.R. of ruptured heart, due to acute cor pulmonale	Hemorrhage from aorta, prolonging surgery
23	22	Recent hemorrhage	Bilateral upper lobe cavities	Segmental resect.	Hypoxia immediately post-op.; *died* 1st day of pulmonary edema	Postmortem showed extensive cavitary disease of RML, RUL
27	26	Advanced bilateral Tbc	Bilateral disease with 6-rib thoracoplasty on right	Pneumonectomy	Pulmonary edema and *death* in O.R. during chest wall closure	Borderline pulmonary function; low blood volume
32	23	—	Cavitary disease with bronchostenosis	Pneumonectomy and 7-rib thoracoplasty	Cor pulmonale, 2nd month; improved following aspiration of pleural fluid	No cause apparent from chart analysis
33	32	Previous RUL lobectomy	Extensive fibrocavitary disease, LUL	Lobectomy	Retained secretions and ventilatory insufficiency requiring tracheostomy and I.P.P.B.; recovered	Should have had tracheostomy immediately post-op.
46	35	Previous LUL lobectomy	BP fistula following previous resection and thoracoplasty	Pneumonectomy	Retained secretions, ventilatory insufficiency and *death,* 2nd day	Should have had early tracheostomy
47	24	Severe laryngotracheobronchitis (Fig. 2)	Giant cavity system, RUL, RLL	Lobectomy plus segmental resect.	*Died,* 3rd day, of pulmonary edema	ACTH given to reduce tracheobronchial disease
51	31	Had drainage procedure for oleothorax, right	Tbc empyema, pneumothorax on left, Tbc extrapleural space infection, right	Pneumonectomy	Progressive ventilatory insufficiency 3 weeks; *died* of pulmonary edema	RML, RLL supplied only vital capacity; should have had tracheostomy and artificial respiration
53	45	—	Cavity, LUL and LLL; post 3-rib thoracoplasty	Lobectomy plus segmental resect. and concomitant thoracoplasty	Ventilatory insufficiency, requiring tracheostomy; *died* 17th day	Should have had tracheostomy earlier, and artificial respiration

TABLE VI HEMORRHAGE AND SHOCK

NO	AGE	OTHER ILLNESS	TYPE OF DISEASE	OPERATION	RESULT	COMMENT
2	17	—	Bronchiectasis RML, RLL	Lobectomy (*bilobectomy*)	*Died* 30 min postop, shock?	No cause apparent from chart analysis
8	32	—	Tension cavity, RUL	Segmental resect	*Died* in O R after postop bronchoscopy, shock?	Possible tension pneumothorax before chest catheters connected to underwater drain
9	32	—	Cavity RUL with Monaldi drainage	Lobectomy concomitant thoracoplasty	*Death* from "shock" 18 hr postop, postmortem miliary Tbc and mucus plugs RMB	Bronchoscopy in postop period might have prevented death
17	23	Malnourished from severe Tbc enteritis	Atelectatic lung	Pneumonectomy	*Died* from shock 3 hr postop	Bleeding extensive and difficult to control at surgery
34	41	"Bleeding tendency"	Cavity, LUL, peel over LLL	*Pneumonectomy*	*Died from shock 5 hr* postop	*Postop* bronchoscopy unsuccessful bleeding poorly controlled at surgery
37	20	—	Destroyed, RUL	Lobectomy	Organizing hemothorax with poor expansion, requiring decortication, thoracoplasty	Cause of bleeding?
38	43	Mod severe essential hypertension	Far advanced bilateral disease, prelim thoracoplasty	Segmental resect	Sudden massive hemorrhage into pleural space, 2nd week, *died*	"Sclerotic PA" noted at surgery
40	44	—	Bronchiectasis, LLL	Lobectomy	Multiple transfusions, thoracentesis, and enzymes required in 1st mo	"Hemorrhage from PA in surgery, controlled by ligature"
42	51	General lethargy, malnourished	Solitary pulmonary nodule	Segmental resect	*Died* suddenly 42 hr postop, postmortem 450 c c blood in thorax	Cause of bleeding?
43	53	Chronic myelogenous leukemia	Cavity and atelectasis of LUL	Lobectomy	Shock immediately postop, *died* in 12 hr despite 2 500 c c blood replacement	Blood dyscrasia not controlled (possible cause)
48	20	—	Far advanced active disease, RUL	Segmental resect	Organizing hemothorax and poor expansion, requiring 2nd operation (decortication)	Cause of bleeding?
52	49	Possible old myocardial infarction	Mixed empyema with granulomatous peel	Pneumonectomy	*Died* in O R, uncontrollable hemorrhage from atrium during dissection	Decortication of calcified peel from pulmonary veins and atrium probably should not have been done
56	35	—	Cavity, RUL	Lobectomy	Shock twice in surgery, postop bleeding required 2nd thoracotomy for clot evacuation	Clamp and suture technique used to develop minor fissure (possible cause)

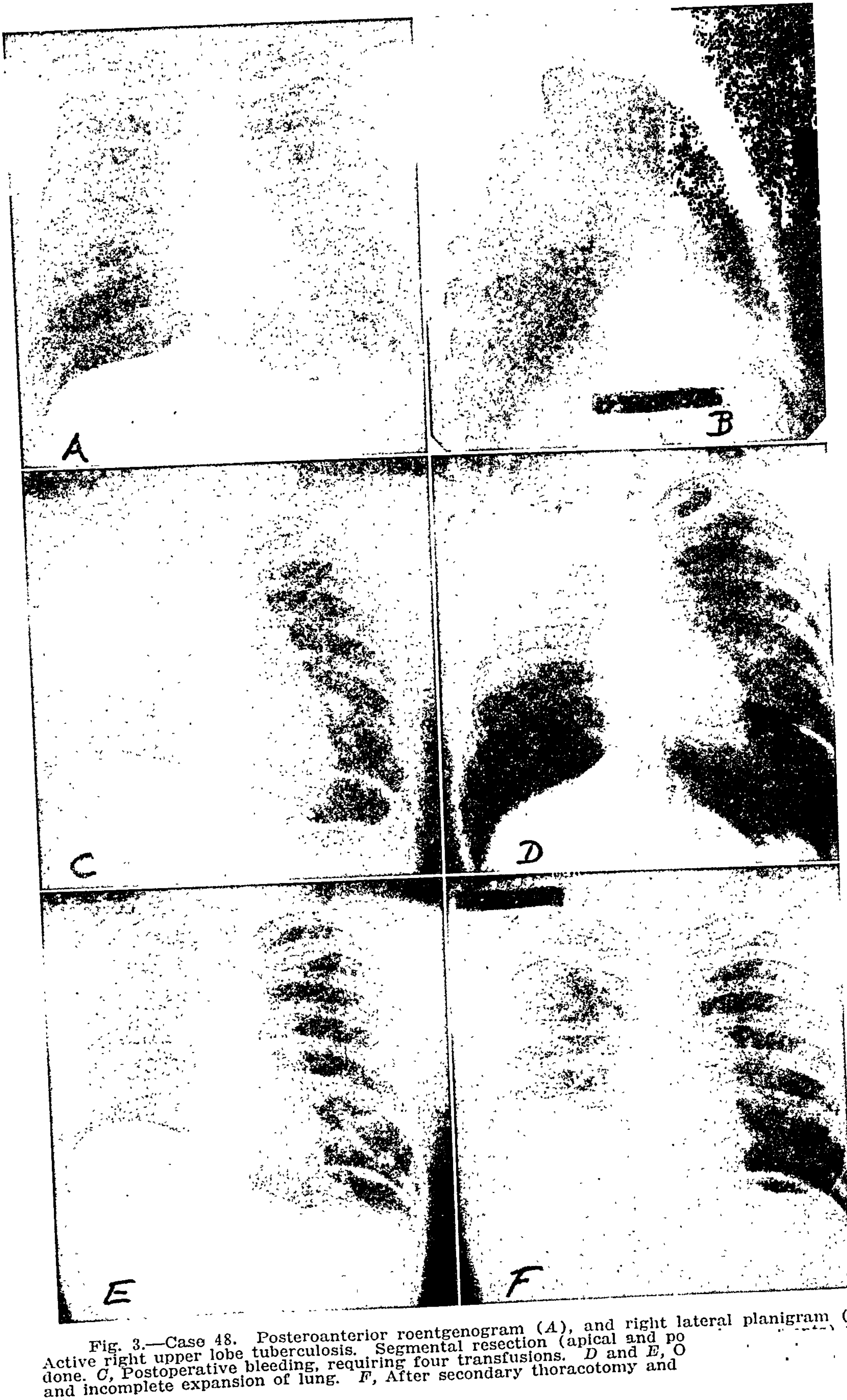

Fig. 3.—Case 48. Posteroanterior roentgenogram (*A*), and right lateral planigram (*B*). Active right upper lobe tuberculosis. Segmental resection (apical and po was done. *C*, Postoperative bleeding, requiring four transfusions. *D* and *E*, O and incomplete expansion of lung. *F*, After secondary thoracotomy and later.

decostalization procedure, but was finally discharged only to develop a paradoxical chest wall later, with poor drainage and bronchiectasis in the right middle lobe This required resection of the middle lobe and several plastic reconstructive operations on the chest wall The case of reaction to local anesthetic occurred in a patient who had had extensive surgery She had had a left pneumonectomy and thoracoplasty in 1950 In 1956 the right middle lobe had been removed, under hypothermia, because of a residual cavity She died following intercostal nerve block for chest pain on the second postoperative day, in which 40 cc

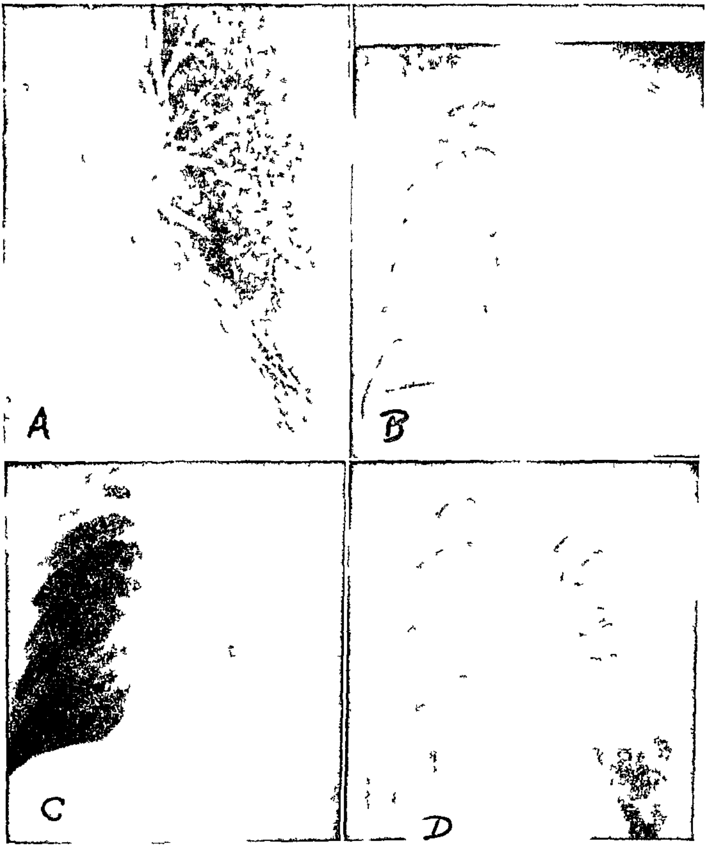

Fig 4—Case 40 *A* Bronchogram showing tuberculous bronchiectasis left lower lobe
B Two days postoperative (left lower lobe lobectomy) hemothorax occurred
C Response to thoracenteses enzymes and transfusions through sixth postoperative week
D Six months later essentially clear chest

TABLE VII. ATELECTASIS

NO.	TYPE OF DISEASE	OPERATION	POSTOP. BRONCHOSCOPY	CAUSE
12	Far-advanced Tbc RUL and superior segment of RLL	Lobectomy and segmental resect.	Yes	Tracheostomy should have been done early in P.O. period, perhaps excess. Pneumoperitoneum (1,500 c.c.)
18	Undiagnosed lesion, RLL	Segmental resect.	Yes	Advanced age (74)—emphysema, asthma
39	Possible Ca (or tuberculoma) RUL	Lobectomy	Yes	Large dose of morphine given 1st night
42	Solitary pulmonary nodule, superior segment of LLL	Segmental resect.	Yes	?
54	Cavity, RLL	Lobectomy	Yes	?
55	Cavity, LUL under thoracoplasty	Lobectomy and segmental resect.	Yes	Excessive secretions noted in surgery; should have had early tracheostomy

of 2 per cent Xylocaine was used. The cases of cardiac standstill are difficult to analyze, as is often the case. However, 1 of these patients had previously had a right lower lobe lobectomy for tuberculosis. The heart stopped during the chest wall closure; resuscitation was at first successful, but cardiac arrest recurred, and she died 1 hour later. She did not have an immediate preoperative bronchoscopy, and the coroner's postmortem examination showed massive atelectasis of the entire left lung. Prior bronchoscopy might have cleaned out the left side better.

There was no significant difference in the number of Negroes who developed complications after resections when compared with white persons who developed complications.

TABLE VIII. CERTAIN COMPLICATIONS RELATED TO KEY DATE, SEPTEMBER, 1952

	BEFORE SEPTEMBER, 1952 (121 CASES)	AFTER SEPTEMBER, 1952 (167 CASES)
Bronchopleural fistula	8 (6.7%)	6 (3.6%)
Empyema	5 (4.1%)	7 (4.2%)
Acute spread of tuberculosis	2 (1.6%)	1 (0.6%)
Pulmonary edema and ventilatory insufficiency	6 (4.9%)	7 (4.2%)
Hemorrhage and shock	5 (4.1%)	8 (4.8%)

PRESENT REGIMEN BASED ON ANALYSIS OF COMPLICATIONS

Commencing in mid-1952, efforts were directed to reduce postoperative complications. That this was at least partially successful is indicated by a comparison of complication rates in the period preceding September, 1952, with the rates from September, 1952, to December, 1956. By reference to Table VIII it can be seen that there were 121 cases of complications before mid-1952 and

167 cases after that date There were 8 bronchopleural fistulas (6 7 per cent) in the early period and 6 fistulas (3 6 per cent) in the later period Of the 3 acute operative spreads of tuberculosis, 2 occurred in the early period and 1 later Since September, 1952, resection surgery has not been undertaken here in the presence of anything suggesting tuberculous bronchitis The percentage incidence of pulmonary edema and ventilatory insufficiency which are considered together, and of hemorrhage and shock, considered together, was approximately the same

Based on these studies and the over all analysis of the complications detailed above, the following plan of care is now standard

In the Preoperative Phase—In addition to stabilization of the patient's lesions by the usual regimen of sanatorium care, cardiopulmonary evaluation is carried out, including electrocardiogram when indicated and pulmonary function tests on all of the patients Careful study of pulmonary function, using well standardized techniques (vital capacity, maximum breathing capacity, minute walking ventilation), together with fluoroscopy, will enable one to predict the likelihood of a patient developing the complication of ventilatory insufficiency Medical consultation is obtained in the borderline cases, and all cases are presented to a combined medical surgical conference before resection is recommended Following the conference, an additional period of observation on the surgical ward is carried out, with the patient ambulatory, preoperative physical therapy instruction is given Estimation of blood volume in patients with chronic suppurative disease is carried out for example in cases of empyema, of destroyed lung, and in all obviously debilitated patients In addition to the conventional and frequently used drugs (streptomycin, para aminosalicylic acid, and isonicotinic acid hydrazide) additional antimicrobials such as viomycin and pyrazinamide are used in cases of drug resistance In the past 5 years it has been our policy to obtain sensitivity studies on all positive cultures When the tests indicate resistance to the "standard" drugs (streptomycin, INH, and PAS), one or more additional drugs are added to cover the surgery Specifically we favor pyrazinamide (in doses of 35 mg/Kg/day) for 1 to 2 weeks preoperatively, and for 6 to 8 weeks postoperatively, with frequent tests of liver function Viomycin is often used, together with pyrazinamide, in cases in which the sputum is resistant to two or more of the standard drugs, in doses of 1 Gm every 12 hours, given on every third day for a similar period of time pre and postoperatively, with frequent tests of kidney function Cycloserine has not been used during the period of study

Bronchoscopy is always done by the surgeons in addition to any endoscopies done at the sanatorium This is done well ahead of the proposed surgery in order to rule out acute or subacute bronchitis the finding of either will cause the operation to be postponed, and preoperative treatment with aerosol, postural drainage, and broad spectrum antibiotics is given Bronchoscopy is also used in the immediate preoperative tracheobronchial toilet of the patient with abundant secretions Bronchography is now done almost routinely this adjunct helps to map the bronchial disease or distortion In addition, plain films and tomograms are studied

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PRESENT REGIMEN BASED ON ANALYSIS OF COMPLICATIONS

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Postoperative observation with removal of the drainage tubes in the first few days, and with all of the above details being carried out, usually leads to rapid re-expansion of the remaining lung. When a space problem exists and cannot be managed by aspirations and intubation, early re-operation is planned. Delayed thoracoplasty for these space problems is an important part of the overall management of the patient. This is usually carried out between 2 and 3 weeks following the definitive resection.

CONCLUSIONS

The role of antituberculosis drugs has been stressed by many workers; we agree that it plays a tremendous part in the prevention of complications in pulmonary resections. The few patients in the series whose sputum contained drug-resistant tubercle bacilli developed serious complications, which is in keeping with findings of other workers. The role of pre-resection or concomitant thoracoplasty is a subject of much debate and, from the present study, the issue is certainly not settled. However, it is concluded that prior or concomitant space-diminishing procedures serve a useful purpose in selected cases, especially when bronchial complications or insufficient pulmonary re-expansion would be anticipated. The color, sex, and age of the patient seem to have little to do with complication rates.

Resection in tuberculosis still carries a higher complication rate than resection for any other pulmonary disease. Reduction in these complications requires meticulous attention to many details by the medical-surgical team which has the patient under observation from the inception of his disease.

Our medical confrères must present to the surgeon a patient whose tuberculosis is stable and not progressive. A negative sputum is desirable but not mandatory. If positive, resistance studies are necessary. The patient's general condition should be as suitable as possible for major surgery. Diabetes, chronic anemia, and heart disease must be controlled or controllable. Patients with low cardiopulmonary reserve must be studied very carefully before planning resection, as emphysema and poor pulmonary function are relative contraindications to extensive resection surgery. From here on the surgeon's responsibility is paramount. He must assure himself of a quiescent bronchus and he must be certain that there is adequate drug coverage should the patient's organisms be resistant to streptomycin, PAS, and INH.

SUMMARY

Two hundred and eighty-eight resections for pulmonary tuberculosis in 274 patients are analyzed. These operations were done over an 11-year period;

they are divided into an early and a late group. The complication rate was 28 per cent for the first 5½ years of our study and 19 per cent for the last 5½ years, which reflects an improvement in surgical technique and in preoperative preparation of the patient with drugs, as well as in careful bronchoscopic study just prior to resection. The causes of the complications are discussed and measures for their prevention suggested. It is believed that the complication and mortality rates can be brought down still lower by the careful preoperative and postoperative management of the tuberculous patient, as well as by meticulous attention to surgical details.

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INTRATHORACIC REDUPLICATION CYSTS

R. N. de Niord, Jr., M.D., Earl T. Owen, M.D., and
Edward H. Hancock, Jr., M.D., Lynchburg, Va.

Duplication or reduplication cysts within the thorax have been thoroughly discussed in an excellent review by Fallon and his associates.[1] These lesions are usually diagnosed at, or shortly following, birth because of obvious respiratory difficulty, including episodic cyanosis, or the occurrence of resistant pneumonia in the early post-partum period.

Duplication cysts usually lie adjacent to and in close association with the esophagus and have been described in all positions within the thorax. However, in one of our cases the large duplication cyst was located immediately posterior to the bifurcation of the trachea causing marked tracheal compression and respiratory obstruction.

Duplication cysts are, by definition, hollow structures possessing a coat of smooth muscle similar to the gastrointestinal tract, lined by mucous membranes, and are usually in close association or communication with a portion of the gastrointestinal tract. These lesions have been described from the base of the tongue to the anus but this paper specifically alludes to intrathoracic duplication cysts. Those cysts occurring within the thorax usually are lined by gastric mucosa which has led to their being called gastric cysts. They contain thick, clear, somewhat viscid material, usually with renin, pepsin, and occasionally hydrochloric acid in high concentration. Accordingly, the pH is low. These lesions may attain rather large size and usually for this reason have associated symptoms of cyanosis due to simple compression of pulmonary tissue. The walls of these cysts become extremely well vascularized whether or not a direct communication with the alimentary tract exists. For this reason dissection must be done with some care because of the rather severe bleeding which may occur.

Gross[2] has described, in his text, thirteen duplication cysts occurring within the thorax. Beardmore and Wigglesworth[3] have related an interesting association of vertebral anomalies and alimentary duplication cysts. We present here 3 cases of duplication cysts within the thorax, in 2 of which there were vertebral anomalies and a large duplication cyst causing tracheal obstruction.

CASE REPORTS

Case 1.—C. E., a newborn infant, had been well until shortly after birth when cyanosis was noted and he was treated for pneumonia. Physical examination was not remarkable except for some diminished breath sounds in the right hemithorax, and diastasis recti.

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X ray studies showed a nonpulsatile smooth mass within the right thorax which seemed to move with the lung on respiration (Figs 1 and 2) The roentgenograms also showed a vertebral abnormality at the level of the fourth thoracic and fifth lumbar vertebrae The hematocrit was 58 Other laboratory studies were normal

At thoracotomy a rather large smooth muscle cyst of the right thorax was found The mass was so large that room for exploration was inadequate After decompression of the cyst by aspiration of 60 c c of clear viscid fluid, several traction sutures were taken in the thick muscular wall and the cyst was easily removed after division of the posterior blood supply from the intercostal vessels The postoperative course was uneventful and the child recovered completely

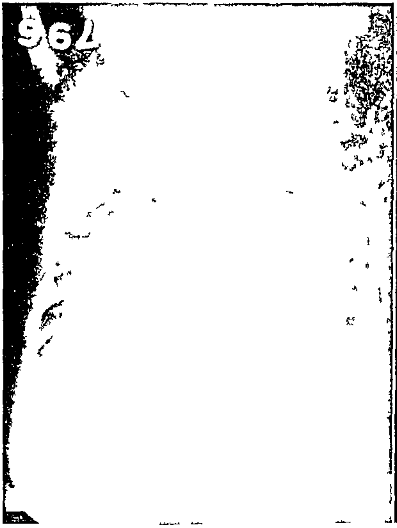

Fig 1

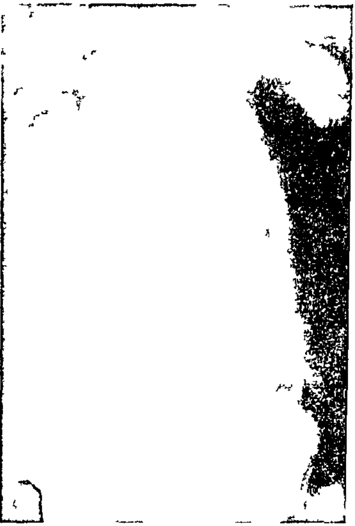

Fig 2

Fig 1 —Case 1 Posteroanterior roentgenogram which reveals a large rounded density in the right lower chest

Fig 2 —Case 1 A lateral projection which shows a rounded density in the posterior basilar region of the thorax which is quite characteristic of duplication cysts

Case 2 —B B, a 19 year old white girl completely asymptomatic, was found on routine x ray study of the chest to have an intrathoracic mass At a left thoracotomy, a large posterior mediastinal mass was found which was thick walled, measured approximately 8 cm in diameter, and appeared grossly to be a duplication cyst This was confirmed at the time of histologic examination Grossly, the lesion was a thick, smooth muscle structure containing gelatinous brown mucoid material which was not foul smelling The external surface of the cyst was extremely vascular, but it was easily removed once the intercostal vessel connections were divided The patient had an uneventful postoperative course

Case 3 —J C, a one week old infant, had been markedly cyanotic with gasping respiration since birth Chest x ray studies revealed bifid cervical and thoracic vertebrae and a rather pronounced mass protruding into the right chest, thought possibly to represent the right heart border The child was so critically ill and short of breath that it was difficult to obtain satisfactory roentgenograms However, a lateral projection was

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association between the enclosure of the spinal cord and notochord by the mesodermal cell mass to form the vertebral body by its anterior fusion, ventral to the notochord and dorsal to the primitive gut In such a closure an adhesion between the ectodermal and endodermal germ layers may occur causing a division of the cephalad growth of *the notochord Thus, a duplication and vertebral* deformity may occur simultaneously

Two of these cases illustrate the importance of decompression of the cystic structure to permit adequate exploration In the third case it was imperative that such decompression proceed rapidly because of the tracheal compression and respiratory obstruction A second common finding is the vascularity of the external surface of such duplication cysts with origin of blood supply from the intercostal vessels This seems to be a common feature and a primary attack on the intercostal communication to the cyst will prevent excessive bleeding

It should be emphasized that in a newborn child with a questionable mediastinal mass, cyanosis and a question of respiratory obstruction, complete x ray studies, including lateral projections, are indicated It has been stated that hemoptysis or excess mucous is a frequent finding in posterior mediastinal duplication cysts due to erosion into the delicate bronchial structures, causing obstructive atelectasis and recurrent infections Early exploration of such lesions by thoracotomy and resection is indicated before such complications occur Newborn infants tolerate operations well and the usual recovery is rapid and uneventful

SUMMARY

1 Spina bifida or defect of the cervical and upper thoracic vertebrae, accompanied by a posterior mediastinal intrathoracic mass in the newborn child appears to be a rather well established syndrome and the diagnosis of duplication cysts can safely be considered

2 The early removal of such duplication cysts or other mediastinal cysts of the newborn is indicated because of recurrent respiratory infections and hemoptysis due to bronchial erosion, and because of cyanosis and obstructive atelectasis with secondary infection Newborn infants tolerate thoracotomy well

3 Three cases of duplication cysts within the thorax are presented In 2 cases there were vertebral body defects and in one case there was almost total tracheal compression with respiratory obstruction All 3 patients underwent successful resection

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SPONTANEOUS SUPERIOR MEDIASTINAL HEMORRHAGE

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Hemorrhage into the superior mediastinum may occur after surgery in the region of the neck, endoscopic procedures, or acute trauma. It also may result from rupture of syphilitic and arteriosclerotic aneurysms of the aorta and its main branches. In all these instances, the etiology can be determined readily by a history of antecedent surgery or acute trauma, and careful evaluation of the aorta by roentgenography.

Two patients have come under our observation presenting a most unusual clinical entity of "spontaneous" superior mediastinal hemorrhage. The etiology in these cases has remained obscure. Their clinical course had an acute onset and was associated with symptoms of progressive increased mediastinal pressure. With supportive therapy, the bleeding stopped, and over a period of several weeks the hematoma disappeared. Subsequent investigation failed to reveal the cause of the mediastinal hemorrhage. These patients have remained asymptomatic, showing no evidence of primary or residual cardiovascular disease.

CASE REPORTS

Case 1.—A 66-year-old white woman, M. F. H., was admitted to the Thoracic Surgery Service on April 2, 1958, complaining of pain and swelling in the right side of the neck. Nine days before admission, the patient had noticed onset of flu-like symptoms: an irritating nonproductive cough, sneezing, coryza, generalized malaise, and headache.

The patient was treated with penicillin without significant improvement. On the night before admission, she developed pain in the right side of her neck which was increased by swallowing and turning her head, and also a dull, intermittent retrosternal ache which radiated to the scapula on the right. There was no vomiting, fever, or chills. The pain increased during the night, becoming severe enough to require narcotics for sedation and analgesia. She complained of increasing difficulty in swallowing and breathing. Three hours later, the patient awoke suddenly and noticed a small, ill-defined swelling in the suprasternal region associated with a bluish discoloration on the right side of the neck. During the next 2 hours, the swelling became more diffuse, extending from both clavicles to the hyoid bone. The patient had been in good health, with no history of syphilis, hypertension, dyspnea on exertion, paroxysmal nocturnal dyspnea, or pedal edema.

The patient was a thin, white woman who appeared anemic. On physical examination, the blood pressure was 120/80 mm. Hg, pulse 70, and the respirations 20 per minute. The neck showed an ill-defined, doughy, diffuse swelling which extended from the suprasternal notch to the hyoid bone. Ecchymosis was present throughout the area. There was point

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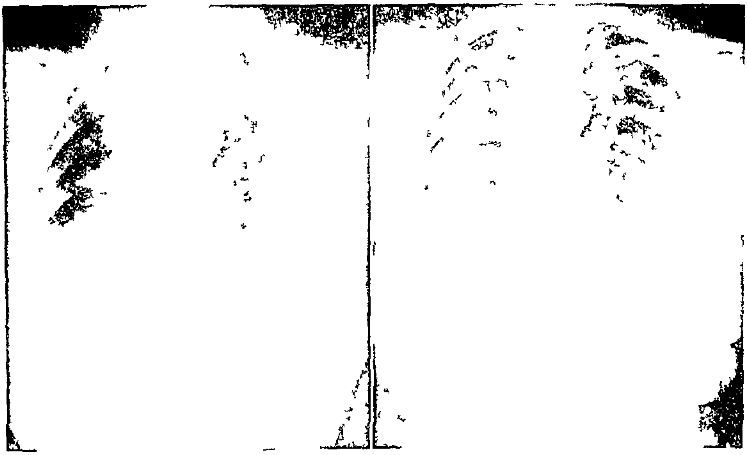
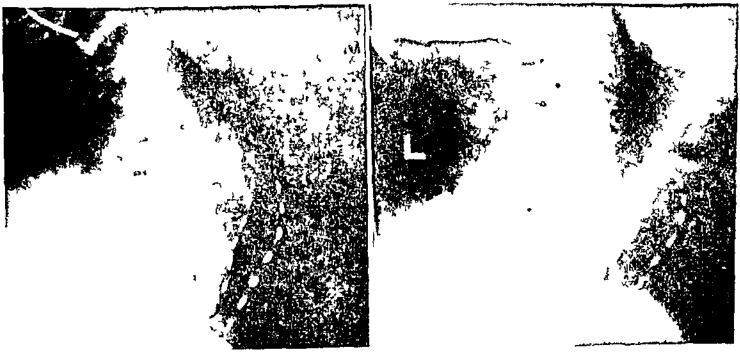
tenderness 1 cm. below and to the right of the thyroid cartilage. No definite thyroid tissue could be palpated because of the swelling. Chest, abdominal, pelvic, and rectal examinations were within normal limits.

The hematocrit was 32 per cent and the white cell count 5,900. The platelet count, bleeding time, prothrombin time, and coagulation time were normal. Serological tests were nonreactive. The blood urea nitrogen was 17, and the blood sugar 117 mg. per cent. Both venous



A B

Fig 1.—*A* Roentgenogram of M. F. H. on admission to the hospital. There is widening of the superior mediastinum without shift of the trachea. *B* The same patient, M. F. H., one year later. The mediastinum is of normal width.



A B

Fig 2.—*A*, Lateral roentgenogram of M. F. H. showing marked anterior displacement of the esophagus and trachea with definite narrowing of the latter. *B* Normal roentgenogram of M. F. H. one year later.

pressure and circulation time were normal. X-ray studies of the chest showed a widened superior mediastinum with anterior displacement of the esophagus and trachea by a homogeneous mass, consistent with hemorrhage into the superior mediastinum (Figs. 1, *A* and 2, *A*).

Vital signs remained normal throughout the patient's hospital course. The patient improved symptomatically, and there was gradual decrease of the neck swelling. Because

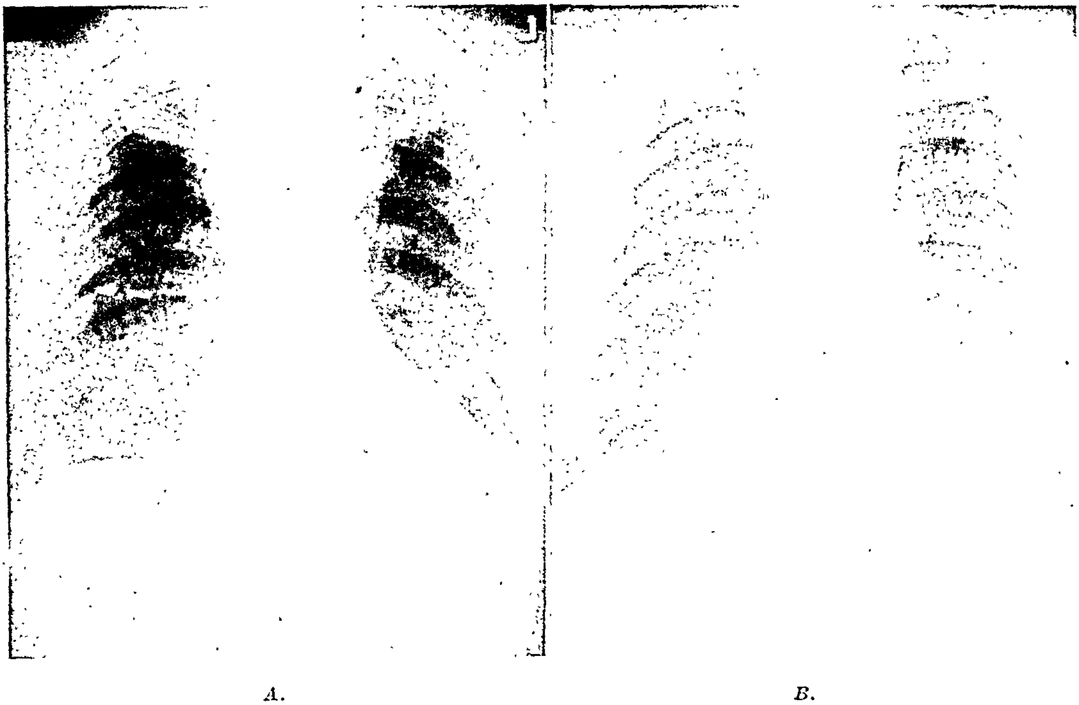


Fig. 3.—*A*, Admission roentgenogram of B. S. There is marked widening of the superior mediastinum without tracheal displacement. *B*, Roentgenogram of B. S. one year later. The mediastinum is of normal width.

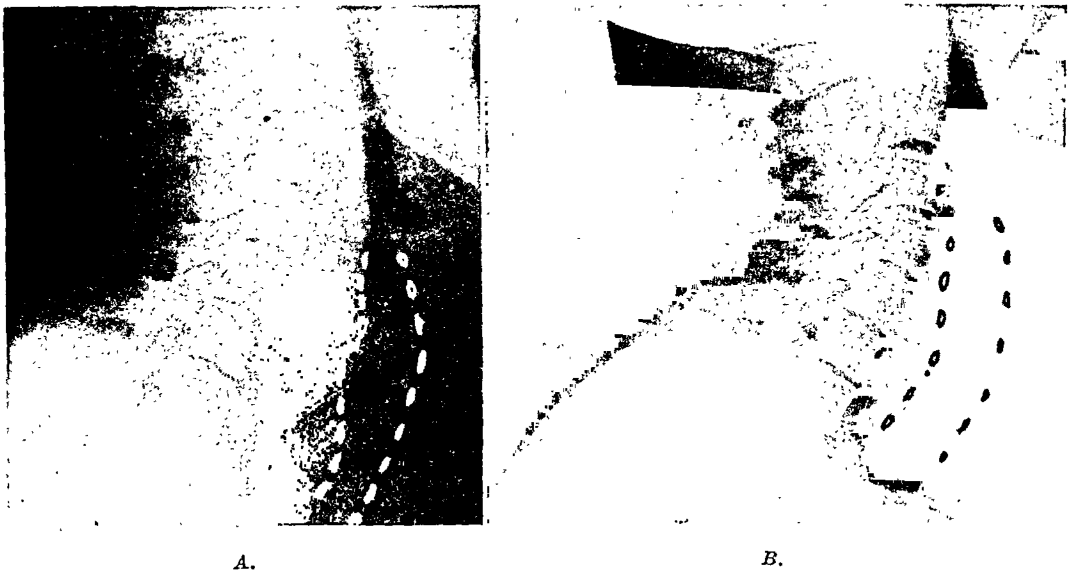


Fig. 4.—*A*, Marked anterior displacement and compression of the trachea on admission of B. S. *B*, Same patient one year later.

of her clinical improvement, exploratory thoracotomy was considered unnecessary During the next few days, the ecchymotic areas became well delineated over the neck and anterior chest with gradual disappearance of all symptoms The patient was discharged on the sixth hospital day, the etiology of her hemorrhage being uncertain

The patient was examined last 1 year later, at which time she had no complaints, and x ray examinations showed a normal neck and chest (Figs 1, *B* and 2, *B*)

CASE 2—A 76 year old white man, B S, was admitted to the Thoracic Surgery Service on July 22, 1958 complaining of chest pain, dyspnea, and swelling in the neck The patient supposedly had had a myocardial infarction in 1942 but since that time had considered himself well, complaining only of occasional burning epigastric pain which was relieved by antacids There was no history of shortness of breath, dyspnea on exertion, pedal edema, paroxysmal nocturnal dyspnea, or hypertension

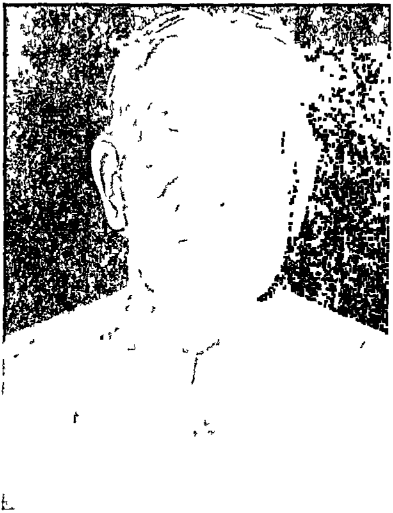


FIG 5—Ecchymosis of neck and upper chest in B S Swelling in neck has subsided although the suprasternal notch is still absent

Several hours before admission, the patient developed a mild crushing discomfort in the precordium which radiated between the scapulas Initially, the pain was not influenced by activity, position change, or deep breathing During the next 3 hours, the pain gradually increased in severity Self induced vomiting and antacids did not relieve his symptoms He began to sweat profusely, became weak and dizzy but did not lose consciousness He began to develop a sense of pressure on both sides of the neck The patient again induced vomiting

This was followed rapidly by a sudden fullness on both sides of the neck For the first time, the pain was relieved During the next 30 minutes, there was a notable increase in the fullness of the patient's neck He was taken to his local physician because of increasing difficulty in breathing, swallowing, and recurrence of his pain Morphine was administered and the patient was fluoroscoped He was told that he might have an aneurysm and was sent to the hospital

Physical examination showed a well-developed, slightly obese white man who was perspiring profusely and was in mild respiratory distress. The patient was alert, although apprehensive, and was not complaining of pain. The blood pressure was 130/60 mm. Hg. The temperature was 96° F., the pulse 65, and the respirations 28 per minute.

Fundoscopic examination showed a slight increase in size of the veins. There was diffuse fullness of the neck, extending from the suprasternal notch to the hyoid bone. Palpation disclosed a diffuse, doughy sensation over the neck, with obliteration of the suprasternal notch. There was no localized mass. The thyroid gland could not be felt and crepitus could not be felt. Both jugular veins were slightly distended. The carotid arteries were full and bounding. Both sides of the chest expanded well. Percussion and auscultation of the chest were within normal limits. The skin of the chest showed a marked delineation in temperature change, being cold and clammy above the nipple line bilaterally with a rather abrupt change to normalcy below the nipples. No murmurs were heard.

The hematocrit was 45 per cent and the white cell count 13,350. The blood urea nitrogen was 15 and blood sugar 117 mg. per cent. Serological tests were nonreactive. The urine showed a specific gravity of 1.020, with a pH of 7, sugar 1+, occasional white and red blood cells. An electrocardiogram showed no evidence of recent or past myocardial infarction.

X-ray studies (Figs. 3, *A* and 4, *A*) showed marked widening of the superior mediastinum with a soft tissue mass displacing the trachea and esophagus anteriorly. The mass appeared to be connected with the arch of the aorta and extended upward into the paravertebral region of the neck. There was no definite evidence of an aneurysm involving the arch of the aorta. Multiple calcifications were present in the thyroid gland, but there was no evidence of intrathoracic extension. The presence of an early dissecting aneurysm was suspected.

With intranasal oxygen and use of narcotics to control pain and restlessness, the patient appeared to improve slightly. Approximately 30 hours after admission, the blood [illegible] dropped to 94/70 mm. Hg, but responded promptly to one unit of whole blood. The pulse varied from 75 to 90 per minute. The swelling in the neck decreased over the next 24 to 48 hours. On the third hospital day, the patient began to show ecchymotic areas around the neck and anterior chest wall (Fig. 5) which became well delineated by the fifth hospital day. Re-examination of the neck after the swelling had receded showed no palpable glands or enlarged thyroid. The patient was sufficiently improved to be discharged on the tenth hospital day.

Since discharge from the hospital, there has been no recurrence of the hemorrhage. A scanogram, employing radioactive iodine, 3 months after discharge showed no abnormal distribution of thyroid tissue. Subsequent x-ray studies obtained 5 and 12 months after discharge (Figs. 3, *B* and 4, *B*) showed complete resolution of the superior mediastinal mass, and cardiac fluoroscopy showed no suggestion of aneurysm.

DISCUSSION

Both patients were admitted to the hospital in acute respiratory distress. There was a history of sudden onset of pain in the neck and substernally, with progressive swelling in the neck. Rupture and dissection of an aortic or arteriosclerotic aneurysm was suspected; however, x-ray evaluation ruled out the presence of such a lesion. There was widening of the superior mediastinum and displacement of the esophagus. This was followed by ecchymosis of the skin at the base of the neck, confirming the diagnosis of superior mediastinal hemorrhage in both cases. In the first patient, severe coughing was considered the initiating factor; in the second patient, vomiting was considered a contributory factor. Both patients responded to supportive therapy and the bleeding stopped spontaneously. In the second case, calcification within the thyroid was considered to be the site of the bleeding. Subsequent examinations failed to demonstrate palpable enlargement of the thyroid gland.

The blood vessels in the superior mediastinum which should be considered as the source of bleeding in these 2 patients are the inferior thyroid, bronchial, and esophageal arteries. One can only speculate as to the etiology of the hemorrhage in these cases. Rupture of a small branch during the violent coughing and vomiting, particularly in the presence of arteriosclerosis, appears to be the only explanation. The slow hemorrhage apparently stopped when the pressure within the mediastinum approximated the systolic blood pressure. Subsequent examinations failed to demonstrate the usual etiological factors responsible for mediastinal hemorrhage of this magnitude.

SUMMARY

Two cases of superior mediastinal hemorrhage of unknown etiology are presented.

The acute mediastinal hemorrhage produced severe neck and substernal pain and was associated with respiratory distress and dysphagia.

Both patients recovered without specific therapy. Examination 1 year later failed to explain the etiology of this "spontaneous" hemorrhage.

THE MARFAN SYNDROME ASSOCIATED WITH AN UNUSUAL INTERVENTRICULAR SEPTAL DEFECT

J. Keith Ross, F.R.C.S., and Frank Gerbode, M.D.,
San Francisco, Calif.

THE ASSOCIATION between the syndrome first described by Marfan,[1] of spider fingers and other skeletal deformities, and cardiovascular disease is well recognized. Bilateral dislocation of the lens[2, 3] became accepted as part of the disease complex 19 years after the original description.

The cardiovascular lesions most commonly met in the Marfan syndrome concern the great vessels, and fusiform aneurysm of the ascending aorta is a frequent finding, with dissecting aneurysm as the lethal complication.[4] The pulmonary artery can also be affected.[5] Apart from the involvement of the great vessels, which is an expression of the heritable connective tissue defect,[6] the Marfan syndrome may be associated with congenital extracardiac defects such as persistent ductus arteriosus, and mild degrees of coarctation of the aorta.[7]

The congenital intracardiac defects most commonly involve the interatrial septum,[7, 8, 9] and, to date, include only one reported example of proved interventricular septal defect.[10] Co-existence with tetralogy of Fallot has yet to be conclusively shown.[7] Patency of the interventricular septum was thought to be present in the case reported by Cockayne,[11] but understandably his clinical diagnosis could not be confirmed by more recently developed techniques.

The purpose of this report is to describe a typical example of the Marfan syndrome in which the diagnosis of interventricular septal defect was proved at open operation. An unusual defect involving an aneurysm of the membranous portion of the septum was successfully repaired with the aid of cardiopulmonary bypass.

CASE REPORT

The patient was a 15-year-old white girl in whom a heart murmur was heard at the age of 6 weeks; she had never been cyanosed and had no cardiac symptoms. She had had four eye operations for dislocated lenses and squint. The family history is incomplete because the mother was adopted at an early age, but there is no suggestion of the disease on the father's side. The mother had noticeably blue sclerae. The patient had one sister, who was normal.

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Physical Examination.—The patient was a tall, slim girl (height 68 inches; weight 121 pounds), with long slender limbs, hands and feet (Fig 1), arachnodactyly, with abnormally mobile fingers, and dorsal scoliosis. She also had a high, arched palate, rather prominent frontal bones, and normally erupted but poor quality teeth. Bilateral dislocation of the lenses was present, with evidence of past eye surgery The ears were normally lobed and normal in shape. Mental development and development of secondary sex characteristics were normal.

Cardiovascular System: The only positive finding was of a Grade 3 pansystolic murmur loudest in the fourth left intercostal space close to the sternal border There was no thrill

Special Investigations: These included a chest roentgenogram (Fig 2); an electrocardiogram, which was normal; and cardiac catheterization

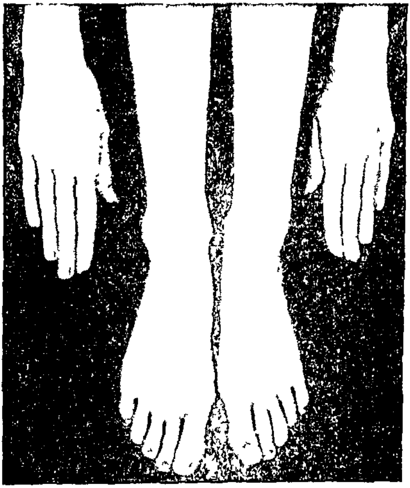

Fig 1—Photograph of patient's hands and feet which demonstrates the long slender extremities The fingers are abnormally mobile

The cardiac catheterization study showed clear cut evidence of a moderate sized left to right shunt at the ventricular level and no atrial shunt Right ventricular and pulmonary artery pressures were normal

Operation—May 19, 1959.—The chest was opened by median sternotomy,[12] significantly more bleeding than usual coming from the skin, subcutaneous tissues, and sternal periosteum.

The ascending aorta and pulmonary artery both looked and felt quite normal. With the patient on cardiopulmonary bypass, the right ventricle was widely opened, revealing what at first looked like a ballooning of the septal cusp of the tricuspid valve. However, the three valve leaflets were then identified and found to be normal, and it became clear that the ballooned tissue was in fact an aneurysm of the membranous part of the interventricular septum (Fig. 3). It was roughly hemispherical in shape when distended, measuring approximately 2 to 2 5 cm across at its base, and had two small holes in its wall inferiorly, through which red blood spurted with each ventricular systole. The right margin of the aneurysm appeared to blend with the adjacent part of the septal tricuspid leaflet and extended for a short distance beneath the leaflet

Fig 2—Photograph of preoperative chest roentgenogram Note rather long narrow thoracic cage and marked dorsal scoliosis There is also prominence of the pulmonary conus and increased vascularity in the lung fields

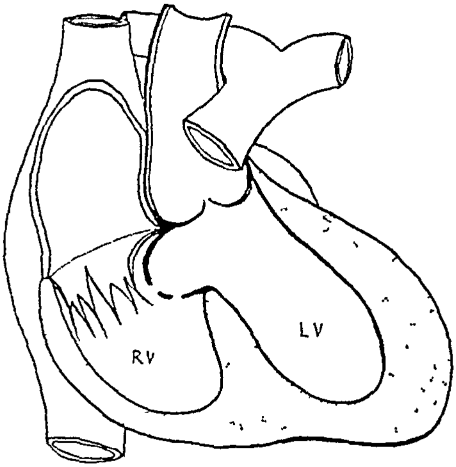

Fig. 3.—Diagram of findings at operation The distortion of the septal tricuspid leaflet overlying the aneurysm is indicated.

The defect was closed by interrupted silk mattress sutures placed through the muscular part of the septum below and the aortic annulus above, the wall of the aneurysm being plicated and incorporated in the repair.

Finally, hypertrophied bands of muscle were excised from the outflow tract of the ventricle and the ventriculotomy was closed, normal heart action resuming when perfusion was stopped. The postoperative course was completely uneventful and wound healing appeared to be normal.

COMMENT

In 1838, John Thurnam[13] pointed out the potential weakness of the membranous portion of the interventricular septum, and described an aneurysm at this site. Unfortunately, Thurnam could give no clinical information except that the heart was "taken from a 'blue boy,' " and as the aortic and pulmonary roots were normal he suggested "some obstruction in the course of the pulmonary circulation" as the cause for the cyanosis

In the present case, while it is tempting to link the connective tissue deficiency of the Marfan syndrome with the findings at operation, there seems little doubt that the septal defect was congenital Thus, the attractive idea of a "blow-out" type of lesion in a previously intact septum, unless it were to have progressed to rupture within 6 weeks of birth, is not tenable If the process were comparable with the stress-fatigue type of change seen in the great vessels it should not have become manifest until early adult life.

It is possible that the membranous septum became secondarily dilated where it was already weakened by the presence of two small congenital defects, but, in the absence of histologic evidence, this must be recorded as an unusual form of congenital interventricular septal defect in an individual who has the Marfan syndrome.

It is also interesting to speculate on the degree of obstruction to blood flow through the right ventricle caused by the systolic bulging of the aneurysm.

SUMMARY

A case is reported in which the Marfan syndrome and interventricular septal defect occur together

A review of the literature shows this to be a rare combination.

The unusual form of the septal defect is described, being a fenestrated aneurysm of the membranous portion of the interventricular septum

The defect was successfully repaired at open operation with the use of cardiopulmonary bypass

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AN UNUSUAL CAUSE OF DEATH FOLLOWING SURGERY FOR VENTRICULAR SEPTAL DEFECT

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THE SURGERY of interventricular septal defects has advanced to a point where treatment of patients with severe pulmonary hypertension is being undertaken. Considerable progress has been made in the development of operative techniques applicable to this special group, notably by Lillehei and his associates. Despite this, the mortality continues to be relatively high after closure of ventricular defects when the pulmonary resistance is markedly increased. In our experience, patients who die postoperatively because of high pulmonary resistance succumb within the first 48 hours; however, we have recently had a case which was an interesting exception to this general rule.

CASE REPORT

The patient, an 8 year old girl, was entirely free from symptoms. A cardiac murmur had been noted first at the age of 6 months during a severe episode of pneumonia. Since that time she had remained well and had been extremely active. She had never been cyanotic.

On examination there was no cyanosis or clubbing. There was a short, harsh systolic murmur, maximal at the second left interspace. The second pulmonary sound was very loud and single. There was a prominent right ventricular heave. Radiographs revealed right sided cardiac enlargement, with pulsating pulmonary vessels that "tailed off" peripherally. An electrocardiogram revealed marked right ventricular hypertrophy, without evidence of left ventricular hypertrophy. Cardiac catheterization with a systemic pressure of 105/70 mm Hg demonstrated a pressure of 95/3 mm Hg in the right ventricle and 94/45 mm Hg in the main pulmonary artery. There was a rise in oxygen saturation from 11.5 volumes per cent in the right atrium to 12.4 in the right ventricle. A femoral artery sample was 96 per cent saturated.

These pressures were confirmed at thoracotomy. A high interventricular septal defect was present which measured about 1½ cm in transverse diameter. Following induced cardiac arrest with potassium citrate, the defect was closed with a compressed Ivalon patch which contained two holes, each 2 mm in diameter. Cardiac resuscitation was uneventful. When cardiac action was satisfactory and with a systemic pressure of 110 (systolic), the right ventricle pressure had dropped to 60 mm Hg. A biopsy was taken from the right middle lobe and was subsequently reported to show severe sclerosis of small arteries. Tracheotomy was performed at the end of the operative procedure. Intermittent assisted respiration was employed in the first 8 hours postoperatively, but did not seem necessary later on.

For the first week the patient's course was uneventful. On the eighth day she began to have intermittent fever up to 104° F. Nothing could be found to account for this at the

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sites of incisions or in chest films. Blood cultures were negative on two occasions. By the tenth day she was complaining of periodic nausea, and the fever continued despite antibiotic therapy. On the twelfth day she became very restless and disturbed, although she had no specific complaints. The following morning she suddenly stopped breathing. Despite resuscitative measures, cardiac action failed about 3 minutes later. The chest was opened promptly, but the heartbeat could not be re-established.

Postmortem Examination.—The pertinent findings were limited to the heart and lungs. In the remainder of the body, the surgical incision in the chest and petechiae of the thymus were the only abnormalities.

The parietal and visceral layers of the pericardium were covered with a thick shaggy layer of fibrin. A 4 cm. suture line had been placed in the pulmonary outflow and there were also two small areas of suturing in the right atrium, one of which fastened a patch of fibrous tissue to the outer surface.

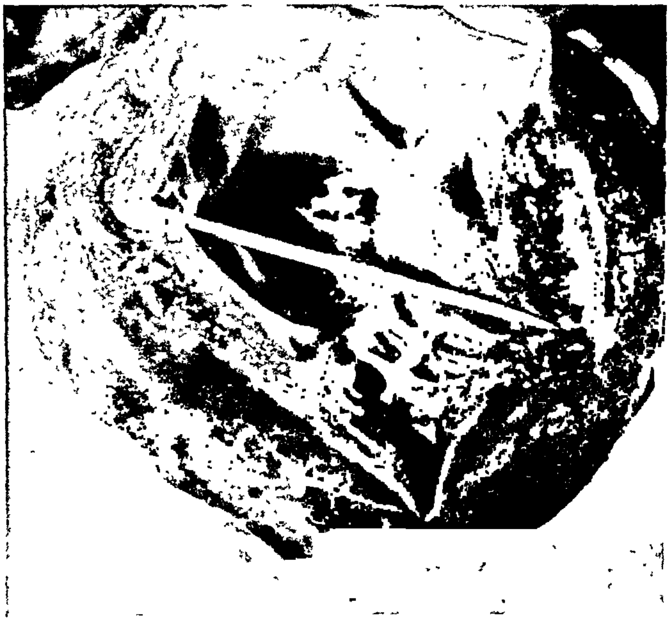

Fig. 1.—Heart–the right ventricle has been opened to display the perforated Ivalon sponge sutured into the ventricular septal defect. The right ventricle is markedly hypertrophied and the pulmonary artery widened.

The heart weighed 350 grams. The wall of the left ventricle measured 1.4 cm. in thickness, the right 0.8 cm. The upper end of the interventricular septum contained a round 1.5 cm. defect which had been closed by means of an Ivalon sponge perforated by two small holes (Fig. 1). A few tiny petechiae surrounded the patch. The myocardium underlying the sutures was yellow and necrotic, otherwise the muscle was firm and red-brown throughout. The tricuspid and mitral valves were normal. The aortic valve and aorta measured 4 cm. in circumference; the pulmonary valve and pulmonary artery measured 6 cm. Small yellow flecks of atheroma streaked the aorta, particularly above the valve, and somewhat smaller blemishes were found in the pulmonary artery. The coronary vessels were normal. The pleural cavities contained a trace of fluid. The lungs weighed 320 and 250 grams, respectively, and were moderately congested. The branches of the pulmonary artery were large and stood out prominently.

Microscopically, the hemorrhages in the thymus and necrotic foci adjacent to the incision in the myocardium were confirmed. The lungs showed patchy edema and alveolar hemorrhages. The striking pathologic changes were confined to the arterial tree. The large elastic arteries were normal, but some of the smaller ones were nearly occluded by pads of loose fibrous tissue. The media was somewhat thickened and contained very occasional foci of foreign body giant cells. The muscular arteries were involved by a severe necrotizing inflammation which extended through the entire wall and into the surrounding tissues (Fig. 2) Only short segments of the vessels and sometimes only an arc of the circumferences were affected, but serial sections demonstrated that practically every large muscular artery was involved at some point. The arterial wall was swollen with edema and heavily infiltrated by polymorphonuclear leukocytes and a rare eosinophil. The outer adventitia contained a dense accumulation of lymphocytes and plasma cells and large pale cells resembling reticulum cells. The intima was thickened by a layer of edematous fibrous tissue, the internal elastic lamina was often

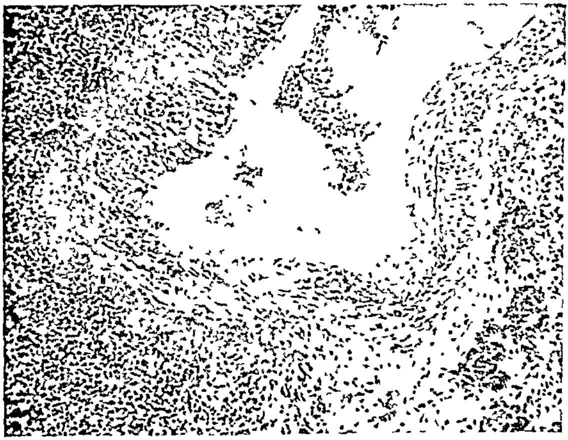

Fig 2 —Acute arteritis in muscular pulmonary artery Only a segment of the vessel is involved There is some older intimal fibrosis (Hematoxylin and eosin; X110)

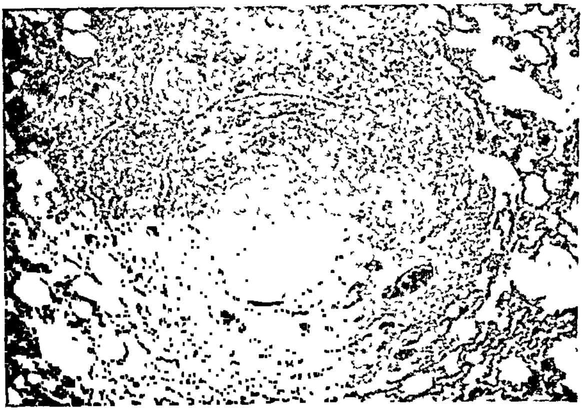

Fig. 3 —Healing arteritis in muscular pulmonary artery. Fibrin and some inflammatory cells are still present in the wall *The same lesion was frankly acute in another area on serial sections.* (Hematoxylin and eosin; X35)

partly smudged, and the muscle fibers of the media were disrupted and widely separated. Extravasations of fibrin and frank hemorrhages had occurred into the media and sometimes the adventitia. Crescentic sinusoidal vessels, consisting only of a single layer of endothelial cells and containing a small amount of blood, partly encircled the inflamed congested portions of the vessels. Nearly all the lesions were acute and appeared to be only about a week old. In the odd artery, however, the inflammation was giving way to the healing phase (Fig. 3). Young granulation tissue was growing in and repairing the damaged regions. These more advanced lesions always merged with an area of active inflammation and were estimated to be between 2 and 4 weeks old.

The smaller branches of the arterial tree occasionally showed a spillover of the inflammatory process, but mainly displayed the changes characteristic of prolonged severe pulmonary hypertension. While some of the small muscular arteries and arterioles were thick-walled and showed fibrous occlusion of the lumen, many others contained fusiform or globular dilatations filled with endothelial cells and organizing thrombi which divided the lumen into multiple tiny capillary channels, the whole complex being drained into the capillary network by means of one or more large, thin-walled vessels, lined only by endothelium and elastica. Occasionally a few foreign body giant cells lay in the middle of the proliferating endothelium. The veins and remaining organs were histologically normal.

COMMENT

Pulmonary arteritis may occur as an isolated phenomenon or as part of a generalized disease, either a hypersensitivity reaction or periarteritis nodosa. When the process is confined to the lungs, it is always associated with raised ulmonary artery pressure. The underlying disease may be mitral stenosis, congenital heart disease with a shunt, or essential pulmonary hypertension.[1-3] Because of those instances in which the pulmonary hypertension is clearly secondary to some cardiac defect, it is now generally conceded that the arteritis is the result of the high pressure and not the cause of it.

The case reported here resembled the others in the literature in its clinical course and pathologic findings. The interesting feature was that the arteritis apparently developed after occlusion of the cardiac shunt. The child had been in good health prior to surgery and the immediate postoperative course had been uneventful. Only 6 days before death an abnormal unexplained degree of fever and, later, some respiratory difficulties had given cause for concern. These symptoms can undoubtedly be attributed to the onset of the widespread arteritis. In the majority of cases previously reported, the disease ran a fulminating course, lasting only a few days.

The absence of arteritis in the lung biopsy taken at the time of the cardiac repair, although seemingly confirmatory, is really inconclusive evidence. This biopsy specimen contained only a few small peripheral arteries, while the inflammation involved mainly the larger muscular vessels and even those were only affected in short segments. However, the bulk of the lesions at the postmortem examination were acute and obviously of recent origin, well within the 2 weeks which had elapsed since surgery; even those which were healing could have developed since the operation.

The occurrence of the arteritis in the postoperative period can be explained in two different ways. First, its manifestations at that particular time may have been purely coincidental. Heath and Edwards[1] have recently described the step like evolution of hypertensive changes in the lung vessels, in their classification arteritis constitutes the highest grade Our patient displayed all the other degrees of severe damage and might have just been ready to pass into the arteritic phase It is unlikely that the operation caused a permanent lowering of the pulmonary pressure and thus prevented the development of arteritis since, in patients in whom the vasculature has become as rigidly sclerotic as in ours, the hypertension is maintained by the fixed resistance in the lungs, even after correction of the cardiac malformation [5]

Alternately, it is possible that the operation triggered the onset of the arteritis If one assumes that a right to left shunt existed, closure of the ventricular septal defect could have raised the pulmonary pressure by obstructing some of the outflow from the right ventricle Two small holes were left in the Ivalon sponge in order to allow gradual adjustment to the altered hemodynamics, but these were perhaps too small to be effective Some facts speak against the presence of a right to left shunt the patient was never cyanosed and preoperative catheterization actually demonstrated a small left to right shunt and, immediately after closure of the defect, the right ventricular pressure fell On the other hand, the occasional patient has been described in whom a right to left shunt was unaccompanied by cyanosis [6] Moreover, such severe sclerotic lesions as were seen in the lungs of our patient are nearly always associated with a right to left shunt [5] The small volume of the left-to right shunt during catheterization does not exclude the possibility of a reversal of flow at other times Even the postoperative lowering of the pressure in the right ventricle might be misleading evidence in view of the unphysiologic conditions under which the pressures were taken Once the arteritis had developed it must have led to further hypertension by aggravating resistance in the lung and, thus, a vicious circle was established

SUMMARY

In a child with a high ventricular septal defect and marked pulmonary hypertension, the defect was closed by means of a perforated Ivalon sponge The first postoperative week was uneventful but then a widespread fatal arteritis developed in the lungs An attempt is made to explain this complication on a physiologic basis

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JUNCTION BOX FOR VIEWING DIFFERENT LEADS ON TWO CARDIOGRAPHS OR CARDIOSCOPES DURING SURGERY

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During open-heart surgery at this center (pump-oxygenator or hypothermia), the cardiologist frequently has wished to view an electrocardiographic lead on his oscilloscope different from the lead preferred by the anesthesiologist on the latter's oscillograph. Heretofore the only equitable solution to this problem was to attach double sets of leads to the patient, as running one cardiac monitor from the pre-amplifier of another necessitates viewing the same lead simultaneously on both instruments. Double leads are unsatisfactory in that too many wires adorn the patient, and—in the case of needle electrodes—eight rather than four punctures are required.

A small junction box has been constructed to permit simultaneous recording or observation of two different electrocardiographic lead patterns on two (same or) different types of apparatus, recording and/or monitoring, while only one set of leads is attached to the patient. Parts are few and of standard variety obtainable anywhere. The principle is division of each extremity lead into two within the box, while maintaining continuity of isolated shielding through and within the box. Standard phone plugs and jacks are used as quick connectors on both input and output sides.

The box itself is made of ¼ inch plywood; a metal box might permit water to condense inside, with consequent voltage drop across components within the box. Input connections may have any type of patient terminal, needle or plate, as the shielding of the cable is dead-ended at the terminal. Needle electrodes modified by the authors from the design of Brehm[1] are used at this hospital (Figs. 3 and 4).

Output connections from the junction box to whatever monitors one wishes to use, whether cathode-ray oscilloscopes or direct-writing oscillographs, are easily made by affixing phone plugs to the lead wires provided with any monitor in place of the terminals ordinarily provided, as shown in Fig. 5 where a Grass Polygraph* and a Sanborn electrocardiograph† are the two monitors to be used.

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*Model 5 Polygraph, Grass Instrument Co., 101 Old Colony Ave., Quincy, Mass.

†Model 51 Viso-Cardiette, Sanborn Co., Waltham, Mass.

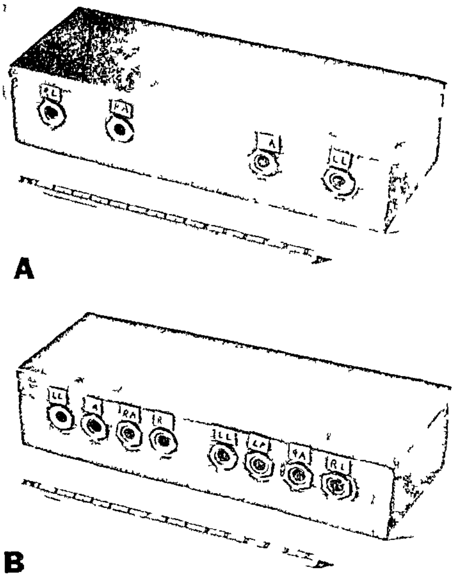

Fig 1 —Input (A) and output (B) sides of the junction box

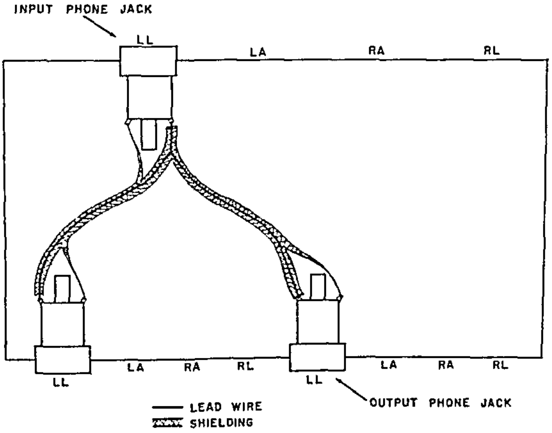

Fig 2 —Diagram of each patient lead splitting into two within junction box with preservation of shielding

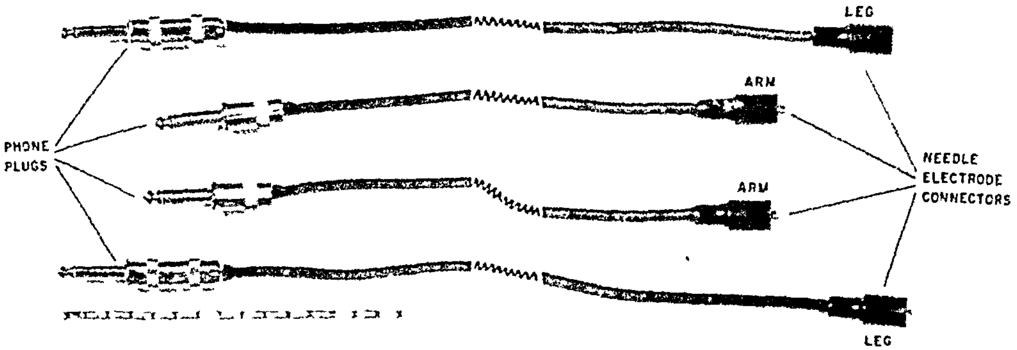

Fig. 3.—Leads from extremities of patient to input side of junction box Leg leads are 9 feet long, arm leads 6 feet

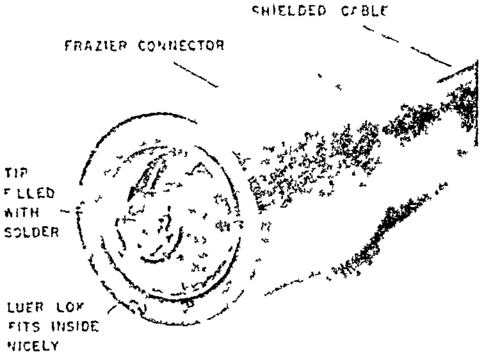

Fig 4—Detail of needle electrode Luer connector, modified from design of Brehm.[1]

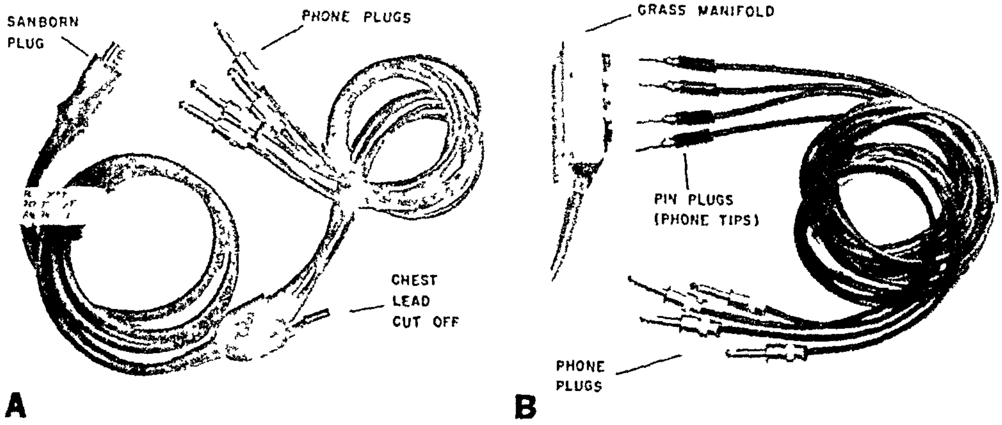

Fig 5—*A*, Standard Sanborn electrocardiographic patient cable, retaining usual Sanborn 5-pin male plug, but with Sanborn lead terminals replaced by phone plugs.

B, Connections to Grass Polygraph, showing phone tips for insertion into Grass pin jack manifold, and phone plugs for connection to junction box.

If the two monitoring devices have their chassis connected to ground, each will record without interference from the other, and the choice of lead shown on or written by each machine is completely free for the operator of each. Changing leads on one monitor causes only a momentary deflection in the oscilloscope trace or written record of the other. In the operating room, the junction box may conveniently be secured with adhesive tape on or near the head of the operating table.

SPECIFICATIONS

	Junction Box
Phone plugs	I C A No 27, shielded, long or short
Phone jacks	I C A single *open circuit No 1870*
Shielded cable	Sanborn Co, Waltham, Mass. Part No. 2160-A
	Other Apparatus
Frazier connector	Codman & Shurtleff Co, Boston, Mass., connector for combined suction and coagulation in electrosurgery
Phone tips	Standard solderless pin plugs
Sanborn input cable	Sanborn Part No 651-99
Luer connectors	(from broken syringes), Becton, Dickinson & Co, Rutherford, N. J.

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DISSECTING HEMATOMAS OF INTRAPULMONARY ARTERIES IN A CASE OF PULMONARY HYPERTENSION ASSOCIATED WITH PATENT DUCTUS ARTERIOSUS

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Multiple dissecting hematomas of the large intrapulmonary branches of the pulmonary arteries developed following transection of a patent ductus arteriosus in a patient with severe pulmonary hypertension. No similar lesion has been revealed in a survey of the literature.

The structural changes of pulmonary vessels in pulmonary hypertension have been studied. Steinberg[1] described pulmonary arteriosclerosis in 83 per cent of 35 cases of mitral stenosis. Brenner[2] concluded that the average degree of sclerosis of pulmonary vessels was greater in the group of patients with pulmonary disease and hypertension than in the group with disease of unknown etiology. Pulmonary vascular sclerosis has also been observed in congenital cardiac abnormalities associated with pulmonary hypertension. More recently Heath and Whitaker,[3,4] by recording pulmonary artery blood pressure by cardiac catheterization, have been able to correlate the arteriosclerotic changes in the pulmonary vessels with the degree of pulmonary hypertension. Studying patients with mitral stenosis, Goodale and co-workers[8] did not find a close relationship between the degree of pulmonary sclerotic changes and the degree of pulmonary hypertension.

Dissecting aneurysms of the trunk of the pulmonary artery are extremely rare.[5,6,7] In each of the cases, the aneurysm involved only the trunk of the pulmonary artery and the dissecting aneurysm had burst into the pericardium. Durno and Brown[6] reported a patent ductus arteriosus in a 33-year-old man with a tear of the intima at the bifurcation of the trunk of the pulmonary artery.

In the case to be described it is suggested that pulmonary hypertension and severe atheromatous degeneration of the pulmonary vessels are predisposing factors of the dissecting hematomas.

CASE REPORT

A 36-year-old white housewife was referred to the University of Kansas Medical Center, 2 months before death, for evaluation of dizziness and polycythemia. Her past

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history revealed a diagnosis of heart disease of undetermined etiology since childhood For many years she had noticed coldness and cyanosis of the hands when they were held above her head Approximately one year before death the patient noticed the onset of "dizzy spells" which progressively increased and caused her to faint occasionally

On admission, the patient was well developed and nourished but had cyanosis of the fingernail beds and oral mucosa The arterial blood pressures were 110/80 mm Hg There was no clubbing of the fingers

The chest was clear to percussion and auscultation There was a Grade 2, split second sound in the pulmonary area and at the apex There was a Grade 2 diastolic blowing murmur along the left sternal border No other murmurs were heard The remainder of the examination was negative The temperature of the patient was normal throughout her hospital stay

Hematocrit was 74 5 per cent, hemoglobin 15 6 Gm , white blood cells 4,450 Serum electrolytes were carbon dioxide, 27 mEq per liter, sodium, 139 mEq per liter, potassium, 4 2 mEq per liter Roentgenograms of the chest showed a prominent pulmonary outflow tract, increase in the vascular markings of the lungs and right heart hypertrophy Electrocardiograms suggested right ventricular hypertrophy

Ear lobe oximetry at rest disclosed a saturation of 92 per cent and a decrease after exercise to 89 4 per cent After 100 per cent oxygen inhalation for 3 minutes the patient's oxygen saturation was 94 8 per cent

A right heart catheterization showed a patent ductus arteriosus The catheter was passed through the aorticopulmonary communication into the descending aorta There was a marked pulmonary hypertension equal to the descending aortic pressure No fall in pulmonary artery pressure occurred after acetylcholine administration or 100 per cent oxygen inhalation

One week before death the patient underwent a thoracotomy The patent ductus arteriosus measured 1 5 cm in external diameter and 0 7 cm in length During the operation the right ventricular pressure was 90 mm Hg while the systemic pressure was 90/55 Temporary occlusion of the ductus for 10 minutes resulted in an immediate fall of the right ventricular pressure to 40 mm Hg while that in the aorta was 80/50 mm Hg Upon release of the clamp, the right ventricular pressure returned to its previous level Accordingly it was decided to transect the ductus The patient recovered satisfactorily from the general anesthesia

During the immediate postoperative course, the right ventricular catheter which had been left in place revealed a steadily rising right ventricular pressure The catheter was removed after 24 hours at which time right ventricular pressure was 150 mm Hg During all this time the systemic arterial blood pressure was 80/60 mm Hg The pulse rate increased progressively from 60 per minute on the day of surgery to 160 per minute on the day before death Systolic arterial blood pressures ranged between 90 and 68 mm Hg and diastolic 54 to 60 mm Hg Respiration varied from 20 to 24 per minute

During the postoperative course the hemoglobin was 13 3 Gm per cent, hematocrit 38 per cent, and the white blood count 22,000 The urine output varied from 175 c c on the day of surgery to 1,800 c c the day before death Electrolytes were within normal limits Roentgenograms of the chest showed the lungs to be expanded, and an increase in bronchovascular markings throughout both lungs as compared with the films taken before operation The third postoperative day, the patient became progressively dyspneic, coughed frequently, and expectorated moderate amounts of bloody mucus

On the following days she had several episodes of marked dyspnea, associated with severe chest pain, restlessness, and shock She was placed in an oxygen tent, tourniquets applied, and aminophylline given These measures produced some objective and subjective improvement but the patient continued to be markedly dyspneic and eventually died Postoperative electrocardiograms showed sinus tachycardia, right bundle branch block, and first degree atrioventricular block In the last electrocardiogram taken 2 hours before death there was complete atrioventricular dissociation, and a ventricular rate of approximately 140 per minute

Gross Findings.—At autopsy the body measured 1.54 meters in height and weighed 54 kilograms. There was a 15 cm. healing left thoracic incision at the level of the fifth intercostal space. The fifth rib was absent.

The heart weighed 420 grams. The right ventricle and auricle were dilated and hypertrophied. The right ventricle ranged from 7 to 10 mm. in thickness. The left auricle and ventricle and the coronary arteries showed no abnormalities. The cusps of the pulmonary valve were normal. The pulmonary and aortic stumps of the transected ductus arteriosus were sutured.

The intima of the trunk and main intrapulmonary branches of the pulmonary artery showed many elevated, irregular yellow patches measuring from 1 to 5 mm. in diameter. In the large branches the intima betwen the plaques was irregularly opaque. The atherosclerosis was more marked in the main right and left intrapulmonary branches and to a lesser degree in the smaller branches. The plaques were more numerous and large at the points of arterial branching causing, at times, narrowing of the lumens. There was neither calcification nor ulceration of atheroma.

Several large arteries of the right and left lung showed extensive dissection of their walls by recent hematomas. This resulted in varying degrees of narrowing of the lumens of the involved arteries. In general, the dissecting hematomas extended along the vessel and its branches. The points of intimal rupture were difficult to determine by gross inspection.

The dissecting hematomas involved all of the main intrapulmonary branches of the right upper lobe, one of the main branches of the lower left lobe, and one main branch of the right lower lobe. The pulmonary parenchyma adjacent to the dissected arteries showed hyperemia. The pulmonary arteries of the right middle lobe and upper lobe of the left lung were not involved by hematomas. A few ante-mortem clots were found in a main arterial branch of the middle lobe and in a few small arteries of the upper and lower lobes of the left lung. There were two small hemorrhagic infarcts approximately 2 cm. in diameter in the upper lobes of the lungs.

Atelectasis was moderate in the left lower lobe, and slight in the right lower lobe of the lungs. There were also fibrinous adhesions between the left lung and the parietal pleura.

The remaining organs did not show significant abnormalities.

Histologic Studies.—To study both large and small vessels, sections were taken from all lobes of the lungs, both from near the hilus and from the periphery. The sections were stained with hematoxylin and eosin, Verhoeff-van Gieson, toluidine blue, oil red 0, and Masson connective tissue stains. Sections from the heart and abdominal organs were stained with hematoxylin and eosin and Verhoeff-van Gieson stains to study the systemic vessels elsewhere in the body.

The findings in various sections from the elastic pulmonary arteries (diameter greater than 1,000 μ) were similar. There was a marked, irregular intimal thickening of part or of the entire circumference of many arteries. The thickened intima was made up of dense hyaline fibrous tissue. Some patches consisted of a loose fibrillar connective tissue with few ovoid and spindle-shaped cells. Varying amounts of fat were present in most of the patches. Beneath some of the larger atheromatous plaques the media was thinned; elsewhere the media was thickened and showed an irregular increase of connective tissue. In numerous places the media showed irregular foci of faintly blue metachromatic material, and still in other places small cysts, some of which were confluent. The elastic tissue was in general absent or fragmented in the patches of atheroma. No infiltration of inflammatory cells was seen in any of the arteries examined. The adventitia showed no abnormalities.

The small muscular pulmonary arteries showed marked thickening of the intima with narrowing of the lumen. The thickened intima consisted of dense hyaline connective tissue with few spindle cells. Fat was absent in the sections examined.

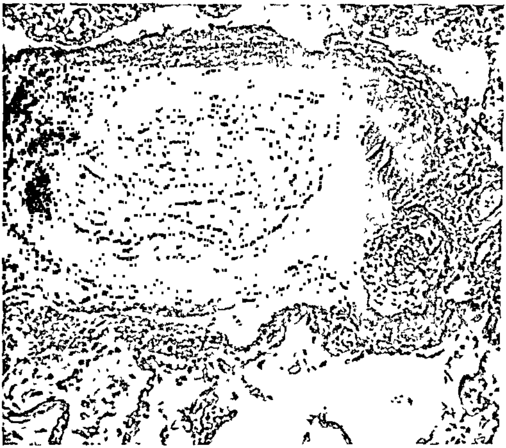

Fig. 1.—Pulmonary arteriole occluded by recanalized thrombus (Verhoeff-van Gieson stain; × 100.)

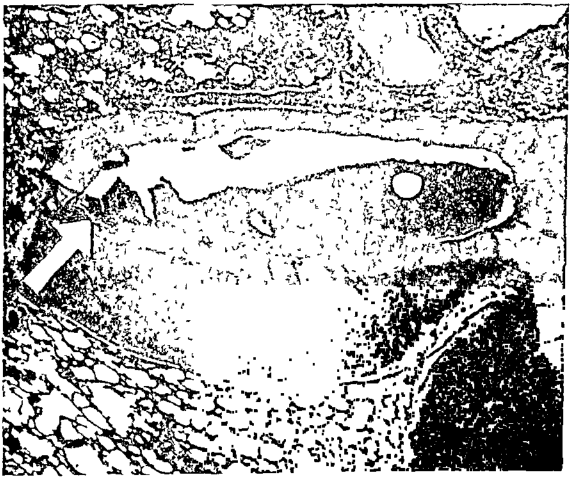

Fig. 2.—Artery showing a large intimal tear (*arrow*) through which the blood has dissected between the media and adventitia. Right lower corner shows extension of the dissection into the adjacent branch. (Hematoxylin and eosin stains; × 36.)

Extensive pulmonary arteriosclerosis associated with severe pulmonary hypertension is considered to be the main pathogenic factor.

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ARTERIOVENOUS FISTULA OF THE LEFT INTERNAL MAMMARY VESSELS SIMULATING A PATENT DUCTUS ARTERIOSUS

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ARTERIOVENOUS FISTULAS of the thoracic wall are rare Even more unusual are fistulas involving the internal mammary artery, only 2 cases of which were reported from the vast array of injuries sustained in World War II Shumacker and Carter[1] reported 1 case and the second was recorded by Walter Reed Army Hospital[2] Both of these fistulas involved the right internal mammary artery and innominate vein A third case, which followed radical mastectomy, was reported by Glen and Steinberg[3] This was an arteriovenous aneurysm involving the right internal mammary artery and vein

The lesions reported above were not confused with patent ductus arteriosus However, Maier and Stout[4] reported a case of an arteriovenous fistula of the left acromiothoracic and lateral thoracic arteries and the adjoining veins which did simulate this condition Their preoperative diagnosis was simplified when a mass developed in the left subpectoral area

In the case we are about to present neither of these happy circumstances existed, that is, a history of a penetrating injury or the presence of a mass It was our firm conviction that the patient had a patent ductus arteriosus and little thought of an arteriovenous fistula was entertained until the left thoracic cavity was opened

CASE REPORT

The patient was a 35 year old white male telephone lineman who was told in 1955, following a routine physical examination, that he had a heart murmur This was found on all subsequent physical examinations, and one doctor, who had examined him several times, thought that the murmur was growing louder He had some shortness of breath on exertion and during the previous several months had noticed that he could not keep up with his co workers in doing heavy work His main purpose in entering the hospital, however, was for investigation of left temporal and frontal headaches which he also had had for the previous 6 or 7 years In 1944, the patient had had a left mastoidectomy, and in 1958 an operation on the left shoulder for removal of some calcium He had had a rather severe injury to his left chest in 1951 when he fell from a telephone pole

On physical examination, the patient was a well developed, well nourished white man in no apparent distress He had a scar over the left mastoid area and a scar over

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the left shoulder. There was a machinery-like murmur over the left second parasternal interspace which was confined to an area about 2 inches in diameter. There were no other abnormal physical findings.

The routine laboratory studies were all normal and pulmonary function studies were better than predicted. While in the hospital he was seen by members of the Ear-Nose-Throat, Eye, and Neurological Departments, none of whom could ascertain the source of the headaches. The members of the medical department thought that he might have an aneurysm of one of the cerebral vessels but this was never confirmed. A right heart and left pulmonary artery catheterization was performed and found to be normal.

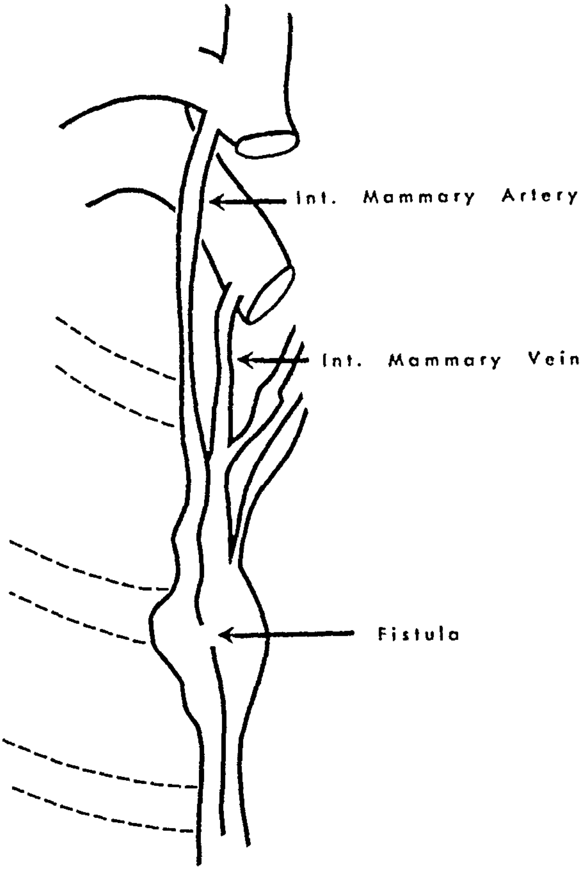

Fig. 1.—The arteriovenous fistula of the left internal mammary vessels as viewed from behind.

Since no obvious cause for the headaches could be determined, correction of the patent ductus arteriosus was considered to be in order. Accordingly, on April 27, 1959, the patient was operated upon through a left posterolateral thoracotomy incision. It soon became evident that there was an aneurysm involving the left internal mammary artery and vein and that a patent ductus arteriosus did not exist. Fig. 1 illustrates the anatomy as found at the time of surgery. It was thought that the procedure of choice, as recommended by Holman,[5] was ligation of the artery and vein proximally and distally and excision of the entire fistula. This was performed without any difficulty. No thrill was felt in the area of the ligamentum arteriosum. However, it was also isolated, ligated, and divided.

The patient developed a pericardial friction rub following surgery but this faded in about 5 days. The murmur disappeared and he was discharged from the hospital on the eleventh postoperative day.

DISCUSSION

In retrospect it seems unlikely that this murmur, which was rather loud but confined to a small area, could have been missed in the many examinations this man had prior to and after induction into the service during World War II. The additional history of injury to the left chest with the advent of the murmur several years later suggests a traumatic rather than congenital etiology of the fistula.

The patient has not had a headache since surgery which must be accepted as a pleasant but fortuitous sequela.

As an oddity the case is interesting, and with the increasing number of crush injuries to the anterior chest due to automobile accidents, similar phenomena may be observed more frequently in the future.

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INNOMINATE ARTERIOVENOUS FISTULA

A Report of One Case and Review of the Literature

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ARTERIOVENOUS FISTULA between the innominate vessels is exceedingly rare and presents some unique problems in diagnosis and treatment. There have been 7 cases of innominate arteriovenous fistula previously reported in an extensive literature on the general subject which originates with the recognition of this abnormality by William Hunter in 1757.[1] Major contributions to our understanding of the regional and systemic hemodynamics and reactions of the patient or animal to an arteriovenous fistula have been made by Holman,[2] Reid,[3] Elkin,[4] and Lillehei.[5]

There follows a case report which details the diagnosis and treatment in the eighth reported case of innominate arteriovenous fistula.

CASE REPORT

F. T., A-72589, aged 26, was admitted to the Ancker Hospital on April 17, 1959, 30 minutes after being shot in the left neck with a .32 caliber bullet. The bullet passed from the left cervical region to the region of the right axilla posteriorly. A right pneumothorax, mediastinal hematoma, contusion of the right lung, and fracture of the third rib on the right posteriorly were found on admission (Fig. 1). A thoracostomy tube was inserted after which the lung expanded. Serial measurements of cervical circumference over the first 48 hours following admission revealed an increase of only 2.5 cm. This decreased gradually after 48 hours. The patient was repeatedly examined for a thrill and bruit because of the likelihood of vascular injury with a missile which passed from one side of the body to the other across the superior mediastinum. A thrill and bruit were first detected on the ninth post-injury day. This was accompanied by an increase in pulse rate to 120 per minute from 80 to 90 prior to this. The patient complained for the first time of shortness of breath on walking to the bathroom. The murmur which was continuous was heard with maximal intensity over the right sternoclavicular joint and was transmitted into the right cervical region. The murmur could be heard over the entire precordium and into the epigastrium. Peripheral pulses were equal and no neurologic defect was elicited on examination.

A diagnosis of arteriovenous fistula involving the innominate vessels was made. The following confirmatory procedures were done. (1) Cardiac catheterization, (2) venous and arterial angiograms, (3) venous pressures of both upper extremities, and (4) circulation times (arm-to-tongue) with injection into the antecubital vein of both arms.

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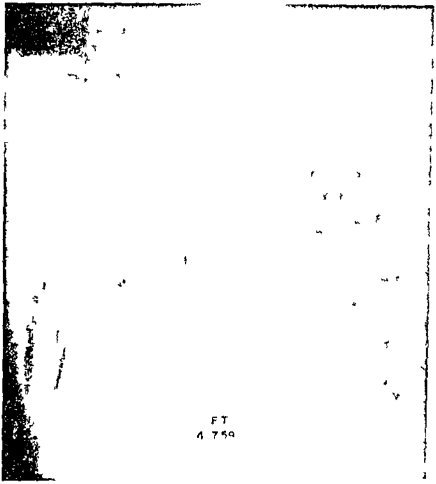

Fig 1—Chest roentgenogram of patient at time of admission which shows right mediastinal hematoma and pneumothorax. The bullet [illegible] in the right axilla

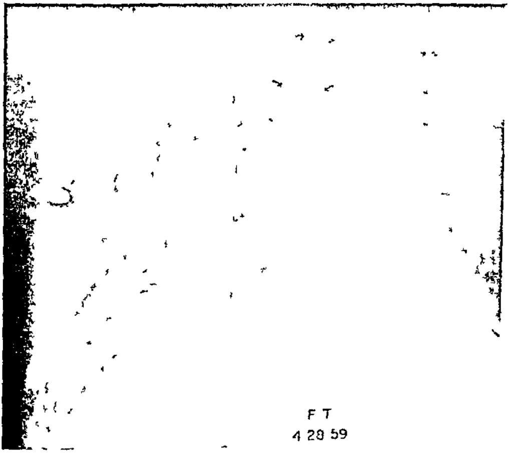

Fig 2—Arterial angiogram which shows injection made via a catheter the tip of which is placed [illegible] artery. A collection of contrast material outside of the artery which di[illegible]s circulation is outlined by small arrows. This proved to be a fal[illegible] The upper arrow is pointing to contrast material in the common

The electrocardiogram was normal.

Veno-cardiac catheterization revealed a large increase in oxygen saturation in the right innominate vein. An increase in pressure also occurred at this point (Table I). The arterial angiogram revealed a collection of dye outside of the innominate artery which in retrospect was in an associated false aneurysm between the innominate artery and right innominate vein (Fig. 2). An insufficient quantity of contrast material was injected to visualize the fistula in this area. Venous angiography likewise did not make the fistula visible. The venous pressures and circulation times (Table II) indicated involvement on the right side.

Operation was performed on May 8, 1959 (3 weeks following injury), with the use of hypothermia. The patient was cooled to 90° F. The electroencephalogram of the patient

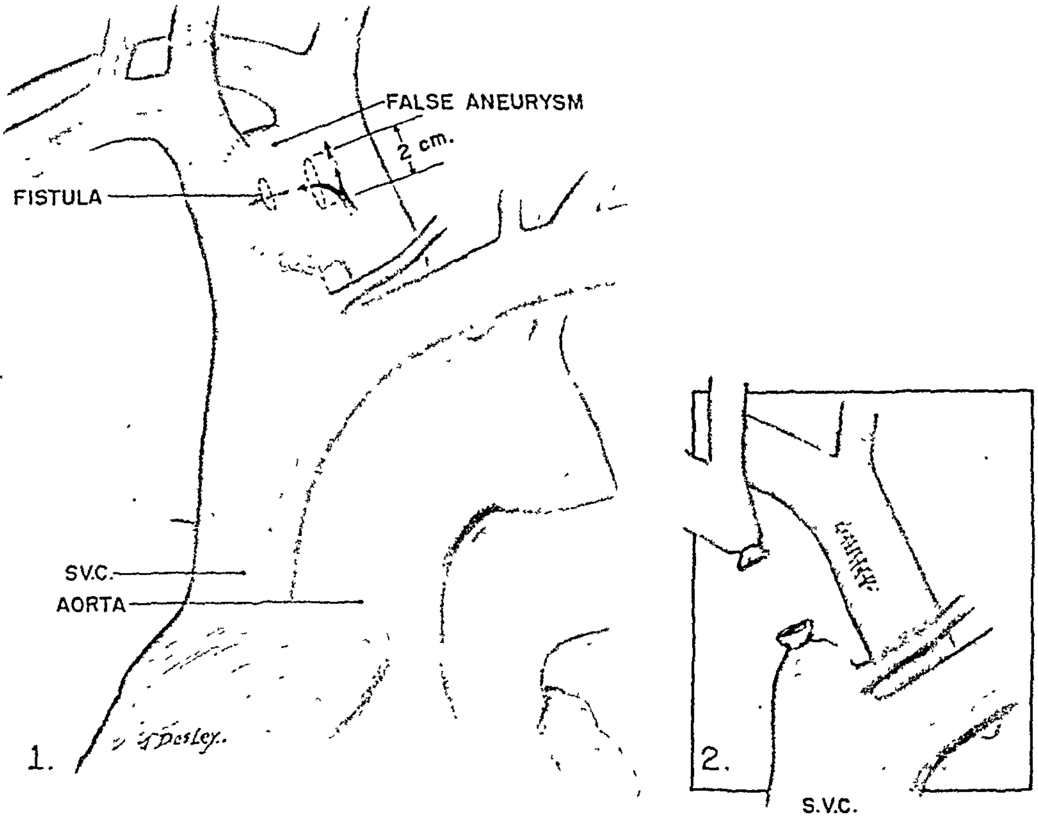

Fig. 3.—The false aneurysm and fistula as visualized at the operation. The right innominate vein was closely adherent to the false aneurysm and both were resected. The innominate artery was controlled cephalad to the left innominate vein. The completed repair appears at right.

Table I. Data Obtained From Veno-Cardiac Catheterization

	MEAN PRESSURE (MM. HG)	O_2 SATURATION (PER CENT)
Brachial vein	—	67
Subclavian vein	16	74.0
Right innominate vein	24	92.9
Left innominate vein	6	63.2
Superior vena cava	5	83.4
Main pulmonary artery	20	63.21
Femoral artery		93.44
Right ventricle	15	—

Cardiac output = 10.31 L./min.
Cardiac index = 5.34

TABLE II VENOUS PRESSURES AND CIRCULATION TIMES PRIOR TO SURGERY

DATE	ARM	VENOUS PRESSURE (CM)	CIRCULATION TIME (ARM TO TONGUE) (SEC)
April 27, 1959	Left	12 4	14 0
	Right	20 0	19 0
May 4, 1959	Left	10 0	12 0
	Right	21 0	20 0

was monitored throughout the procedure The incision extended from the suprasternal notch to the fourth intercostal space The sternum was divided longitudinally over that distance and the incision was extended out into the fourth intercostal space on the right The sternum was separated and adequate exposure resulted without resection of any portion of the clavicle The thymus was resected and tapes were placed about the right and left innominate veins and the innominate, carotid, and subclavian arteries A thrill was easily palpable with maximal intensity in the right innominate vein The innominate artery was separated from the right innominate vein by a false aneurysm (Fig 3) The right innominate vein was intimately associated with the false aneurysm Repair was accomplished by temporarily occluding the innominate artery proximal to the fistula and the carotid and subclavian arteries distal to the fistula A lateral defect in the artery 2 2 cm in length, was repaired without narrowing the lumen The false aneurysm 4 cm in diameter, was excised with the adherent right innominate vein The innominate artery was occluded for a total of 9 minutes The electroencephalogram did not change during innominate carotid, and subclavian artery occlusion The patient has had normal carotid and radial and brachial pulses since surgery and no thrill or murmur has been detectable He was discharged from the hospital on May 21 1959 the twelfth postoperative day, and has returned to work since that time as a dining car waiter

DISCUSSION

The previous experience with innominate arteriovenous fistula is summarized in Table III The first reported attempt at surgical repair was by Lexer in 1934[6] Since that time 6 additional cases have been reported[7 11] A loud, usually continuous, murmur was found in all patients Definite cardiac failure had developed in 5 of the patients prior to treatment An interval of over 1 year existed between injury and treatment in these patients The arteriovenous fistula communicated between the innominate artery and the right innominate vein in 3, the left innominate vein in 3, and the junction of the right and left innominate veins in 2 patients

Surgical repair has been quite varied Multiple ligation of the innominate, carotid, and subclavian arteries was performed on 3 patients Closure of the fistula with repair of the artery has been done in 5, either by temporarily occluding the proximal and distal vessels and directly repairing the artery or by transvenous suture after entering the involved vein or by transfixing ligatures through the involved vein using the palpable bruit as a guide There have been 2 deaths among the 8 cases reported The first patient reported died of infection on the eighteenth postoperative day The other death occurred 18 hours following surgery in a patient in severe heart failure with cardiac cirrhosis and ascites The latter patient, reported from the Russian literature,[11] was found to have a small persistent fistula at autopsy The repair was attempted using transfixing ligatures through the involved vein

The region of the innominate vessels can be conveniently exposed by a median sternotomy with extension into the fourth right intercostal space. Direct suture repair of the innominate artery is recommended over other methods previously described.

Venous catheterization with serial measurements of pressure and oxygen saturation of the blood proximal to and beyond the point of suspected fistula is the most convenient method readily available for precisely locating a fistula in this area. Arterial angiography is useful in giving additional information on the presence or absence of an associated false aneurysm.

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ANOMALOUS ORIGIN OF THE CORONARY ARTERIES WITH SPECIAL REFERENCE TO SURGICAL TREATMENT

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ANOMALOUS ORIGIN of the coronary artery from the pulmonary artery has recently been reviewed[1 2] as has ligation of the anomalous vessel in order to improve the myocardial circulation [3] There is still discussion in some quarters, however, as to whether the circulation in these abnormal vessels truly passes from the myocardium into the pulmonary artery Two recent cases may cast some light on this question and therefore are reported

CASE REPORTS

CASE 1 —R E , a 7 year old boy was operated on for closure of an atrial septal defect At the time of exposure of the anterior surface of the heart the right coronary artery was found to arise from the pulmonary artery As the advisability of ligature of this vessel was raised, epicardial electrocardiograms were taken a ligature was passed about the vessel and the vessel was occluded transiently During the time that the origin of the vessel from the pulmonary artery was obstructed it was observed that the vessel became distended and stood out on the surface of the myocardium as though it contained blood under increased pressure as compared to the state prior to its closure On release of the ligature, the vessel decreased in size, appearing as it had prior to manipulation It was concluded that the circulation passed from the normal coronary vessels into the anomalous artery and drained into the pulmonary artery Therefore, the anomalous vessel was ligated at its origin from the pulmonary artery Repeated epicardial electrocardiographic tracings failed to reveal any evidence of ischemia in the region of distribution of the vessel in the myocardium, the atrial septal defect was then closed and the patient's postoperative course has confirmed the fact that no significant damage was done to the myocardium by ligature of the anomalous coronary artery

CASE 2 —C A , a 9 year old boy, was operated on for closure of a ventricular septal defect A rather large anomalous coronary artery was found arising from the pulmonary artery and passing down over the outflow tract of the right ventricle between the normal right and left coronary arteries (Fig 1) The vessel appeared to be the coronary artery of the conus [4] It was dissected free from the myocardium near its origin from the pulmonary artery and a No 22 needle was inserted into its lumen The pressure in the anomalous coronary artery was approximately 32/18 mm Hg, whereas the pressure in the pulmonary artery was about 32/14 mm Hg Both pressures were considerably below the pressure (114/70) in the internal mammary artery When the ligature at the origin of the anomalous vessel from the pulmonary artery was tightened, the anomalous artery became

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tense and distended, standing out from the surface of the myocardium. Simultaneously, the pressure inside of the vessel rose to 100/50 mm. Hg or into the same general pressure range as the systemic arterial pressure and remained at this level until the ligature was loosened. Compared with the pressure originally recorded, the pressure in the anomalous vessel immediately before its complete occlusion suggests that it was partially obstructed. The response to complete obstruction and release was dramatic (Fig. 2). With the ligature released, a 1 per cent solution of Evans blue dye was injected into the anomalous coronary artery, but no staining of the myocardium was observed, apparently because the dye was carried by the anomalous vessel into the pulmonary artery. With the ligature closing at the origin of the anomalous vessel from the pulmonary artery, Evans blue

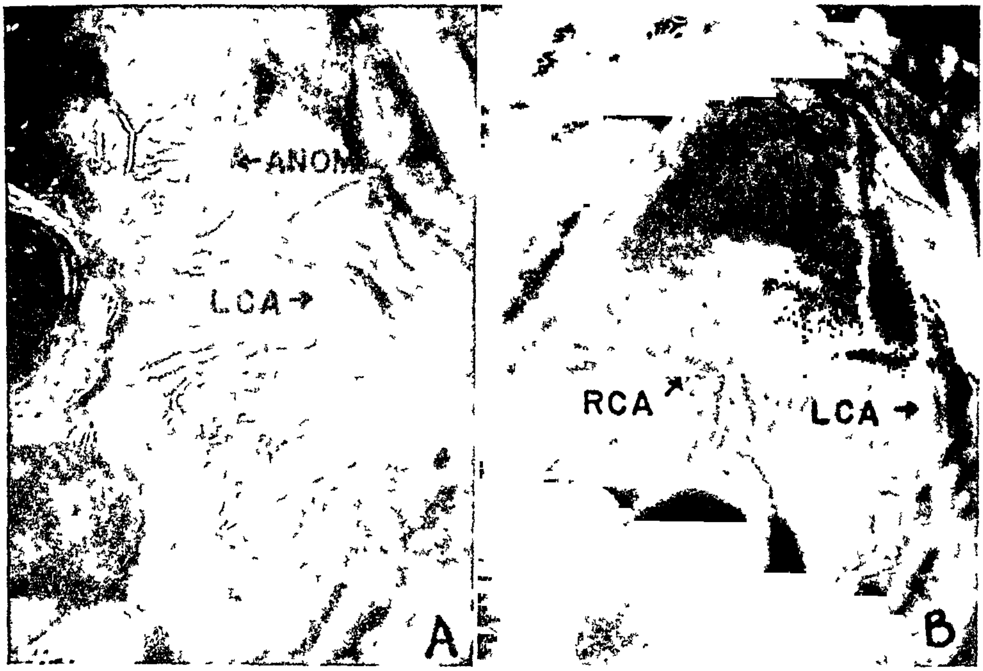


Fig. 1.—These two views show the anomalous origin of the coronary artery of the conus in Case 2. *A* shows the vessel as it arises from the enlarged pulmonary artery and *B* shows its course downward over the outflow tract of the right ventricle between the normally arising left and right coronary arteries.

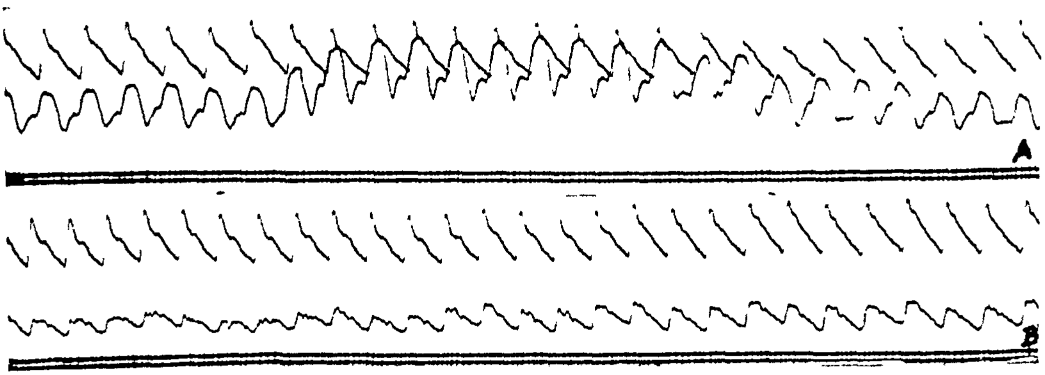


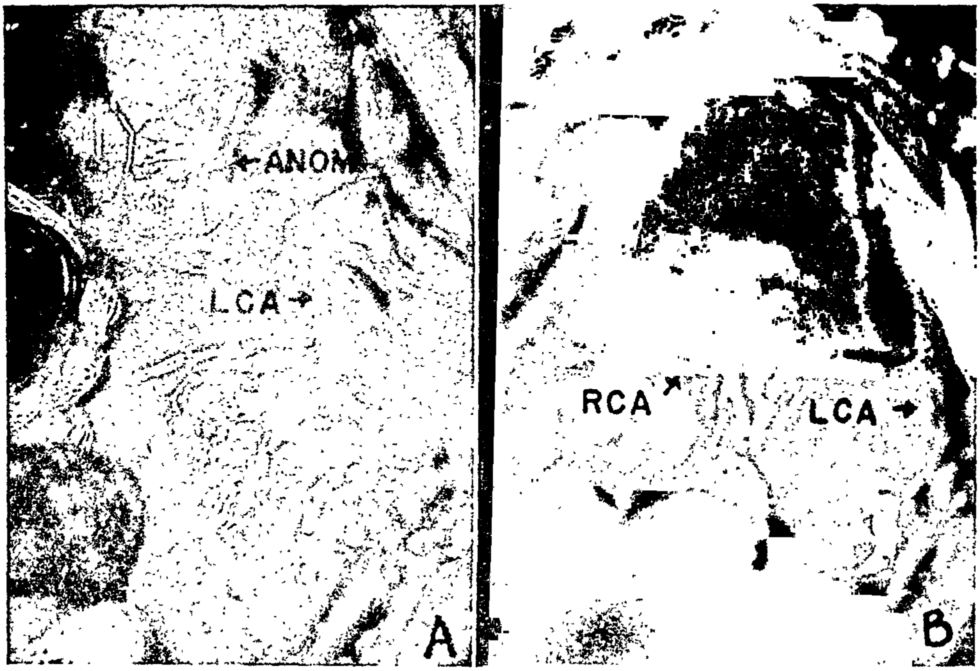
Fig. 2.—*A*, The pressure tracings from within the systemic artery and the anomalous coronary artery are shown during occlusion and release of the coronary artery at its origin from the pulmonary artery. *B*, The pressure tracings from within the pulmonary and the systemic artery. The sensitivity to pressure was the same on all scales throughout. It can be seen that the pulmonary artery pressure was lowest, the anomalous coronary artery slightly higher and the systemic arterial pressure highest. During occlusion of the coronary artery, pressure within its lumen rose toward the systemic arterial pressure level and fell again on its release.

dye was injected again into the anomalous coronary vessel Under these circumstances the Evans blue dye stained the myocardium in the area of distribution of the vessel Furthermore, dye could be seen to pass through anastomoses into the right coronary artery and downward toward the apex of the heart When the ligature was released, the dye was seen to wash out from the stained area of the myocardium and the normal color of the heart returned When the needle was withdrawn from the anomalous vessel, the blood which ran out through the perforation was bright red, in striking contrast to the normal very dark color of blood which has perfused the myocardium It was concluded from this set of observations that the anomalous vessel did not carry blood to the heart but rather drained blood into the pulmonary artery, serving in some respects as an arteriovenous fistula, therefore, it was ligated Observation of the myocardium in the peripheral distribution of this vessel revealed that it remained normal in color and continued to contract forcibly, indicating that the myocardium was not damaged by its ligation Closure of a ventricular septal defect was then performed, and the patient tolerated the procedure well

DISCUSSION

There are several references to the thesis that a coronary artery arising from the pulmonary artery must constitute an arteriovenous fistula because ordinarily it is thin walled and has little pressure at its origin as compared with the pressure at its distal end, where it anastomoses with the arteries which arise from the aorta [3 5 6] Indeed, Brooks reached this conclusion by deduction from pure anatomic evidence in 1885 [5] It is only relatively recently, however, that surgeons have undertaken to ligate anomalous coronary arteries on the assumption that they deprive the myocardium of blood flow [3 8] These attempts have recently been reviewed in a report which presents 2 cases of anomalous origin of the left coronary artery and discusses 3 cases in which ligation of an anomalous left coronary artery was undertaken [3] One of these 3 cases was successful

It is believed that in the 2 cases reported here there is reasonably clear evidence that flow occurred from the myocardium through the anomalous coronary artery into the pulmonary artery The fact that in each case the anomalous coronary artery became distended after ligation indicates that the vessel was filling from normally arising coronary vessels After the ligature had been placed the anomalous vessel was unable to empty into the pulmonary artery as it had previously This is corroborated by the fact that the direct epicardial electrocardiographic leads taken from the area into which the anomalous vessel was distributed in the first case failed to show any evidence of ischemia In the second case, the evidence is even more clear in that (1) occlusion of the anomalous vessel at its origin from the pulmonary artery was associated with a rise in pressure in the vessel approaching the level of the systemic arterial pressure and (2) injection of Evans blue dye into the vessel failed to stain the myocardium in its area of distribution prior to occlusion but did produce immediate staining of the myocardium after the vessel had been occluded at its origin from the pulmonary artery The fact that in both cases the heart tolerated ligation of the anomalous vessel well is further evidence that the blood supply to the myocardium in the peripheral distribution was not compromised by the occlusions tense and distended, standing out from the surface of the myocardium. Simultaneously, the pressure inside of the vessel rose to 100/50 mm. Hg or into the same general pressure range as the systemic arterial pressure and remained at this level until the ligature was loosened. Compared with the pressure originally recorded, the pressure in the anomalous vessel immediately before its complete occlusion suggests that it was partially obstructed. The response to complete obstruction and release was dramatic (Fig. 2). With the ligature released, a 1 per cent solution of Evans blue dye was injected into the anomalous coronary artery, but no staining of the myocardium was observed, apparently because the dye was carried by the anomalous vessel into the pulmonary artery. With the ligature closing at the origin of the anomalous vessel from the pulmonary artery, Evans blue



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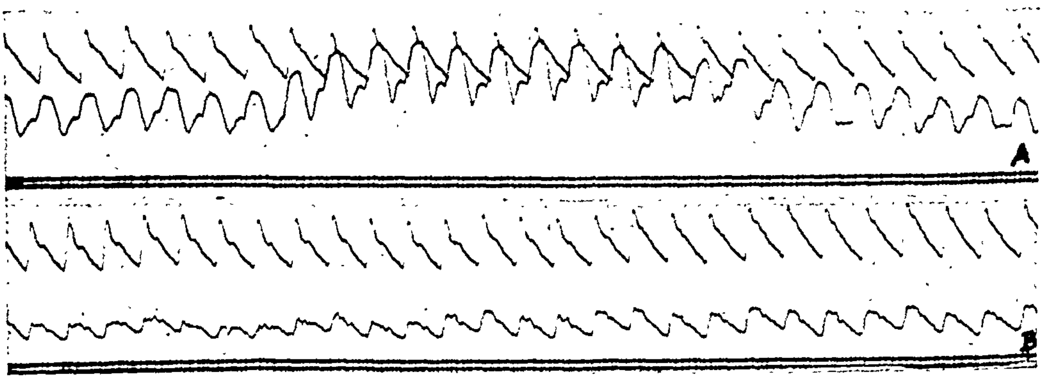

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RENAL AND PORTAL BLOOD FLOW UNDER NORMOTHERMIC AND HYPOTHERMIC CONDITIONS DURING EXTRACORPOREAL CIRCULATION

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TOTAL cardiopulmonary bypass with extracorporeal circulation is being used with increasing frequency in the open correction of cardiac abnormalities Most of those who employ this method attempt to maintain normal body temperature An increasing number, however, are combining moderate hypothermia with extracorporeal circulation because of certain potential advantages of this combination[1 3]

Little is known about the distribution of blood flow during extracorporeal circulation It was the purpose of this study to determine the flow of blood through the kidneys and portal system during total body perfusion with extracorporeal circulation

MATERIALS AND METHODS

Adult mongrel dogs ranging in weight from 14 to 20 kilograms were used They were anesthetized by the intravenous injection of a 5 per cent solution of thiopental sodium An endotracheal tube was inserted and oxygen was administered by means of a mechanical respirator Mid esophageal temperatures were recorded throughout all experiments by means of a telethermometer The mean systemic blood pressure was monitored by means of a plastic catheter placed in a femoral artery and connected with a U tube mercury manometer Cardiopulmonary bypass was accomplished by withdrawing the total vena caval return through catheters by gravity drainage into a bubble oxygenator The oxygenated blood was returned by means of an occlusive Sigmamotor pump into a femoral artery Each animal was heparinized by the intravenous injection of *heparin, 1 5 mg per kilogram* The extracorporeal circuit was primed with fresh heparinized blood Flow rates were

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determined before the bypass was begun by measuring the volume delivered per unit of time. In those animals rendered hypothermic, the body temperature was controlled by means of a heat exchanger and was kept as near 30° C. as possible. Renal and portal flows were measured every 2 minutes during the 30-minute period of study.

Control data concerning cardiac output in normal anesthetized dogs with the chest open were obtained from another study carried out in this laboratory.[1] Similarly, control observations relating to renal and portal blood flows under normothermic and hypothermic conditions were obtained in this laboratory by other studies carried out concurrently.[5, 6]

The method for measuring renal blood flow has been previously described.[7] It permits unimpeded drainage of the total renal venous return by gravity into a graduated burette. The blood is returned by pump into a jugular vein. There is no interference with flow of blood from the infrarenal vena cava into the suprarenal portion of the inferior vena cava. The speed of the pump is so regulated as to return blood into the jugular vein at the same rate as it is being drained from the kidneys. The flow rate is calculated by momentarily stopping the pump and recording the interval of time necessary for the collection of a unit volume of blood.

Portal venous flow was also determined by a method developed in this laboratory and described elsewhere.[6] This method entails division of the main extrahepatic portal vein. Each end of the vein is cannulated with a large-bore plastic catheter. The portal flow is allowed to collect by gravity drainage into a graduated burette and is then returned into the proximal portal vein by a pump which is regulated so that the blood is returned at the same rate as it is being delivered from the distal portal vein. The flow rate is calculated by momentarily stopping the pump and recording the interval of time necessary for collection of a unit volume of blood.

Renal blood flow was measured during total cardiopulmonary bypass in 20 dogs, the temperature of which was maintained at near normal levels. Five animals were perfused at the rate of 40, 5 at the rate of 60, 5 at the rate of 80, and 5 at the rate of 100 c.c. per kilogram per minute. In 15 additional animals, similar studies were carried out at a body temperature of approximately 30° C. Five were perfused at the rate of 40, 5 at 60, and 5 at 80 c.c. per kilogram per minute.

Portal flow was similarly measured during total cardiopulmonary bypass in 15 normothermic dogs. Five animals were perfused at the rate of 40, 5 at 60, and 5 at 80 c.c. per kilogram per minute. In 15 additional animals, similar studies were made in moderately hypothermic dogs. Five were perfused at 40, 5 at 60, and 5 at 80 c.c. per kilogram per minute.

RESULTS

The data concerning renal blood flow are recorded in Table I. Attention should be called to the fact that the control data concerning renal blood flow, and the same is true concerning portal blood flow, were obtained in animals rendered hypothermic by immersion of the body in ice and water rather than by extracorporeal cooling of the blood It is felt that the comparison of data is interesting and informative in spite of the different methods utilized for body cooling Other studies carried out in this laboratory indicate that the chief difference between the two methods concerns a lag in the fall of deep muscle temperature when an animal is made hypothermic rapidly by chilling the blood extracorporeally The drop in temperature of such deep organs, as the liver, is, however, comparable with the two methods

TABLE I STUDIES OF RENAL BLOOD FLOW

	NO OF DOGS	CARDIAC OUTPUT OF TOTAL BODY PERFUSION (C C /KG / MIN)	AVERAGE ESOPHAGEAL TEMP	AVERAGE BLOOD PRESSURE (MM Hg)	RENAL BLOOD FLOW (C C /KG /MIN) RANGE	RENAL BLOOD FLOW (C C /KG /MIN) MEAN	PER CENT OF CARDIAC OUTPUT	PER CENT OF NORMAL FLOW
Normothermic Animals								
Controls	42	126	36 5	130	18 2 35 0	24 5	19 4	100 0
Extracorporeal circulation	5	40	36 7	65	2 7 7 5	5 7	14 3	23 3
	5	60	37 2	94	8 8 15 2	11 6	19 3	47 3
	5	80	36 3	122	11 7 22 7	17 4	21 8	71 0
	5	100	36 5	114	19 2 27 1	22 5	22 5	91 8
Hypothermic Animals								
Controls	10	64	[illegible]	100	7 6 17 2	12 9	19 9	100 0
Extracorporeal circulation	5	40	[illegible]	91	3 5 12 0	6 5	16 0	50 4
	5	60	[illegible]	117	7 0 14 0	10 1	17 0	78 3
	5	80	[illegible]	128	11 7 17 6	14 4	18 0	111 6

It will be noted that the mean systemic blood pressure and the average renal blood flow increased as the total perfusion flow was increased The only exception noted was the mean blood pressure in animals perfused at a rate of 100 c c per kilogram per minute In these animals the mean blood pressure was actually slightly less than in those perfused at 80 c c per kilogram per minute At this high flow rate we had difficulty in preventing some retention of blood in the animal and for this reason this flow rate was not utilized in other phases of the study It will be noted that the average renal flow increased stepwise as the flow rate was increased It was approximately normal with a flow rate of 100 c c in normothermic animals When the renal flow is considered as per cent of total body perfusion, it is evident that this value was only slightly below normal with a perfusion rate of 40 c c and was equal to or slightly above the control value with the higher flow rates When considered as per cent of normal renal blood flow, it becomes apparent that at 40 c c per kilogram per minute the renal flow was only 23 3 per cent of normal This increased at 60 c c to 47 3 per cent, at 80 c c to 71 per cent, and at 100 c c to 91 8 per cent

In the hypothermic animals there was also a linear relationship between the total body perfusion on the one hand and blood pressure and renal blood flow on the other As the flow rate was increased, the blood pressure was elevated and the renal blood flow rose The renal blood flow was about half normal at a flow rate of 40 c.c. per kilogram and was slightly greater than the control value at a flow rate of 80 c.c. When renal flow is considered as per cent of total body perfusion, it is evident that the per cent was only slightly less at the three different flow rates than in the control animals. When viewed as per cent of normal renal blood flow it was approximately half the control value with a flow rate of 40 c.c. per kilogram per minute, in contrast to about 23 per cent in the normothermic animals. At a perfusion rate of 60 c.c., the value was 78.3 per cent, in contrast to 47.3 per cent in the normothermic animals. The per cent was greater than the control with a flow rate of 80 c.c. per kilogram per minute.

Similarly, in both normothermic and hypothermic animals, the mean systemic blood pressure and the average portal flow increased stepwise as the perfusion rate was increased (Table II). The values of blood pressure and of portal flow exceeded the control in normothermic and hypothermic animals at a flow rate of 80 c.c. per kilogram per minute. When portal flow is considered as per cent of total body perfusion it is evident that at each of the three different flow rates under normothermic conditions the percentage of portal flow exceeded that of the control. In the hypothermic animals the portal flow was a somewhat smaller per cent of the total at flow rates of 40 and 60 c.c. per kilogram per minute and was approximately normal at a perfusion rate of 80 c.c. When the portal venous flow is considered as per cent of the normal control values, we find that in normothermic animals at a flow rate of 40 c.c. the portal flow was about one third, at 60 c.c. approximately one half, and at 80 c.c. a little more than the normal. In hypothermic animals at a flow rate of 40 c.c., the portal flow was 42.6 per cent of the normal, at 60 c.c. a little more than three quarters of the normal, and at 80 c.c. 125 per cent of normal.

TABLE II. STUDIES OF PORTAL BLOOD FLOW

	NO. OF DOGS	CARDIAC OUTPUT OR TOTAL BODY PERFUSION (C.C./KG./MIN.)	AVERAGE ESOPHAGEAL TEMP.	AVERAGE BLOOD PRESSURE (MM. Hg)	RENAL BLOOD FLOW (C.C./KG./MIN.)		PER CENT OF CARDIAC OUTPUT	PER CENT OF NORMAL FLOW
					RANGE	MEAN		
Normothermic Animals								
Controls	20	130	36.7	121	20.2-45.9	30.1	23.2	100.0
Extracorporeal	5	40	37.1	75	9.6-12.7	10.9	27.3	36.0
circulation	5	60	37.3	112	10.7-20.2	15.6	26.0	52.0
	5	80	37.0	154	21.1-46.6	33.0	41.3	110.0
Hypothermic Animals								
Controls	10	59.1	28.7	108	12.8-31.6	21.6	36.5	100.0
Extracorporeal	5	40	29.9	102	7.9-11.5	9.2	23.0	42.6
circulation	5	60	29.8	111	11.2-22.5	16.7	27.8	77.3
	5	80	30.1	127	17.1-34.4	27.0	33.8	125.0

Data concerning combined renal and portal blood flows are tabulated in Table III. Regardless of whether the animal was normothermic or hypothermic, both the renal and portal flows tended to be approximately the same at any given flow rate. The combined renal and portal flows in both groups, for example, were approximately 16 c.c. per kilogram per minute at a flow rate of 40 c.c. and approximately 27 c.c. at a flow rate of 60. The mean combined flow was 50.4 c.c. in the normothermic and 41.4 c.c. in the hypothermic group at a perfusion rate of 80 c.c. Combined renal and portal flows at the three different rates under normothermic conditions represented the same or a greater per cent of the total body perfusion than was true in control animals. In the hypothermic group, the combined values for renal and portal flow were slightly less than the control at flow rates of 40 and 60 c.c. per kilogram per minute and represented approximately the same per cent of the total body perfusion when a flow rate of 80 c.c. was used. When expressed as per cent of normal, the combined renal and portal blood flows increased in both groups as the perfusion rate was increased. In the normothermic animals they were 92.3 per cent of the normal at a flow rate of 80, while in the hypothermic group they were 120 per cent of the control at the same perfusion rate.

TABLE III. COMBINED RENAL AND PORTAL BLOOD FLOW

	NO. OF DOGS	CARDIAC OUTPUT OR TOTAL BODY PERFUSION (C.C./KG./MIN.)	COMBINED RENAL AND PORTAL FLOW (C.C./KG./MIN.)	PER CENT OF CARDIAC OUTPUT	PER CENT OF NORMAL FLOW
Normothermic Animals					
Controls	62	128	54.6	42.7	100.0
Extracorporeal circulation	10	40	16.6	41.5	30.4
	10	60	27.2	45.3	49.8
	10	80	50.4	63.0	92.3
Hypothermic Animals					
Controls	20	61.9	34.5	55.7	100.0
Extracorporeal circulation	10	40	15.7	39.3	46.0
	10	60	26.8	44.7	77.7
	10	80	41.4	51.7	120.0

Our studies showed, in general, a rather linear relationship between the volume rate of total body perfusion, on the one hand, and the mean systemic arterial blood pressure and mean renal blood flow, on the other. It is interesting that the mean renal blood flow and the mean portal blood flow in cubic centimeters per kilogram per minute were almost precisely the same in normothermic animals and in hypothermic animals at any given flow rate. Since the renal blood flow in normal control dogs, rendered moderately hypothermic, is only approximately one half that of normothermic animals and, since portal flow of hypothermic normal dogs is only approximately two thirds that of the normothermic animal, both renal and portal flows at any given flow rate represented a larger per cent of normal control values in the hypothermic animals. A great reduction in total basic metabolic requirements is known to be achieved by rendering an animal moderately hypothermic. These studies would, therefore, lead one to believe that, at any given rate of total body perfusion, the kidneys, splanchnic area, and liver are better supplied with blood with respect to metabolic needs in the hypothermic than in the normothermic state.

Creech and his associates[8] have studied cerebral blood flow during extracorporeal circulation and they also observed a linear relationship between cerebral blood flow and systemic blood pressure. They noted this relationship regardless of the perfusion rate. These observations were further borne out by the magnetic rotometer measurements of cerebral blood flow carried out by Halley and his colleagues.[9] They felt that although there was a good relationship between cerebral blood flow and systemic pressure the perfusion rate itself was an unreliable index of cerebral blood flow. In our own studies of portal and renal flow, we noted a rather good linear relationship between the volume rate of total perfusion, on the one hand, and both systemic arterial pressure and renal and portal blood flow, on the other.

Morris and his co-workers[10] and Beall and his colleagues[11] have studied renal blood flow by indirect methods during extracorporeal circulation in patients. Some of these studies pertain to total body perfusion and some to a measured bypass of arterialized blood into the distal arterial tree during thoracic aortic cross-clamping. In general they were dealing with lower flow rates than were used in our experimental studies. It is interesting, however, that they observed that with perfusion rates of 35 c.c. per kilogram per minute the values for renal blood flow were estimated to be 23 per cent of the control. In our studies in normothermic dogs we obtained similar results. With a perfusion rate of 40 c.c. per kilogram per minute the renal blood flow was calculated to be approximately 23 per cent of the control value.

Our studies are perhaps slightly at variance with those recently reported by Reemtsma and his associates.[12] They observed some reduction below normal in the renal blood flow of normothermic dogs during extracorporeal circulation both at flow rates above and below 50 c.c. per kilogram per minute. They also, however, reported that under these circumstances the mesenteric flow was increased above normal values. In contrast, we found that the portal flow was less than normal both in normothermic and hypothermic animals at flow rates 40 and 60 c.c. Our observations were in agreement with theirs in that at a flow rate of 80 c.c. the portal flow was above normal. This was true both in normothermic and hypothermic animals.

The paucity of postoperative difficulties which might be attributable either to hepatic, splanchnic, or renal damage during clinical cardiopulmonary bypass with extracorporeal circulation would indicate that these organs are ordinarily adequately protected during the period of extracorporeal circulation. It is not known how drastically the normal circulation to these organs can be decreased during a relatively brief interval without consequent damage to them. We do know from other studies that the kidneys are protected adequately by a flow of 7 c.c. per kilogram per minute for a period of 2½ hours.[7] This represents a flow which is approximately one third of normal. One might assume that for shorter periods and under hypothermic conditions a lesser percentage of normal circulation would suffice Nevertheless, it would be wise to err in the other direction Under any circumstances our experimental observations seem to indicate clearly that lower flow rates under hypothermia are comparable to higher flow rates under normothermic conditions with regard to per cent of normal renal and portal blood flow

SUMMARY

Renal and portal blood flows have been measured during cardiopulmonary bypass with extracorporeal circulation In both normothermic and hypothermic animals a linear relationship is observed between blood pressure and renal and portal flow on the one hand and the volume rate of total body perfusion on the other Renal blood flow and portal blood flow are approximately the same at any give perfusion rate in both hypothermic and normothermic animals At any given perfusion rate both renal and portal blood flow represent a higher percentage of normal control values in hypothermic animals than in those which are normothermic

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PULMONARY FUNCTION IN THE IMMEDIATE POSTOPERATIVE PERIOD

Observations of Vital Capacity, Timed Vital Capacity, and Maximum Expiratory Flow Rates in Two Groups of Thoracotomy Patients and a Group of Nonthoracotomy Patients for Seven Postoperative Days

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IN RECENT YEARS, physiologists have made great strides in understanding mechanisms and limitations of the normal lung. Their techniques have been applied to pathologic states with resulting improvement in rational diagnosis and therapy. Most studies in patients following pulmonary resection, however, have been concerned with the long-range results of such therapy. There have been relatively few studies of the immediate results of such surgery, except in the first few postoperative hours or first postoperative day.

This report is part of a program of investigation of the day-to-day changes in pulmonary physiology following thoracic surgery. Using the ear oximeter, Siebecker, Sadler, and Mendenhall[1] showed that there was significant postoperative oxyhemoglobin desaturation in patients who had undergone thoracotomy which lasted up to 8 to 10 days. The most marked desaturation was on the second and third postoperative days. Smith and Siebecker[2] subsequently demonstrated that segmentectomy, lobectomy, and other thoracic procedures were all attended with desaturation, with a tendency to more severe impairment after the more severe procedures. Their results indicated that decrease in diffusing capacity for oxygen and diffuse subclinical atelectasis were not likely mechanisms of the observed desaturation. Mastio and Allbritten[3] and Hood and Beall[4] have demonstrated alveolar hypoventilation with resulting respiratory acidosis in the recovery room and through the first post-thoracotomy day. This report deals with some of the factors that might be responsible for hypoventilation and delineates their changes during the first postoperative week.

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MATERIAL AND METHODS

Seventy-five patients, divided into three groups, were studied. Essential data are contained in Table I. The first subgroup was composed of 24 consecutive patients undergoing thoracic surgery for pulmonary tuberculosis at the Veterans Administration Hospital, Madison, Wisconsin. These patients, all male, had been on anti-tuberculosis chemotherapy and limited activity for several months or more. The majority had segmentectomy or lobectomy to remove residual foci of disease. In addition, there were two pneumonectomies for destroyed lungs, one post-pneumonectomy Ivalon sponge plombage, and one decortication following tuberculous empyema. The second group of 26 consecutive patients underwent thoracotomies for pulmonary tuberculosis at University Hospitals, Madison, Wisconsin. In this group, intercostal neurectomy was practiced at the time of thoracotomy in an attempt to relieve the syndrome of late intercostal neuralgia. Except in regard to sex, this group was comparable to the first as regards age, the procedures undertaken, anesthesia, and postoperative complications

TABLE I PATIENT MATERIAL

	24 THORACIC PROCEDURES	26 THORACIC PROCEDURES WITH NEURECTOMY	25 PERINEAL AND EXTREMITY PROCEDURES
Sex	All male	12 Female 14 Male	16 Female 9 Male
Average age range	37.0 (23–54)	39.7 (20–60)	46.2 (19–74)
Operations	18 Segmental resections 2 Lobectomies 2 Pneumonectomies 2 Others	15 Segmental resections 6 Lobectomies 2 Pneumonectomies 3 Others	13 Vaginal 7 Orthopedic 8 Plastic 2 Urologic
Premedication	Belladonna	Belladonna + opiate	Belladonna + opiate
Anesthesia	N_2O, Thiobarbiturate opiate, relaxant	N_2O, Thiobarbiturate relaxant	18 Inhalation 6 Inhalation + IV 1 Spinal + inhalation
Complications	5 Major respiratory 7 Others	7 Major respiratory 9 Others	1 Major respiratory 1 Major gastrointestinal 17 Others
Deaths	15th postop day	5th postop day	None

The third group, which was included for purposes of comparison, was composed of patients of both sexes undergoing operations on the perineum or the extremities None had significant cardiovascular or respiratory disease and none had pain associated with cough or respiration. All were elective operations for conditions not an immediate threat to life. The average duration of anesthesia for this group was not significantly different from that of the thoracotomy procedures.

Forced vital capacity and timed vital capacity were recorded by the method of Curtis and his associates.[5] Two or more records were taken each day and the largest vital capacity was used. All volumes were recorded at ATPS (ambient temperature and pressure saturated). Records taken from a recording barograph and thermometer during a portion of this study indicate that change to BTPS (body temperature and pressure saturated) or STPD (standard temperature and pressure dry) would not have altered the interpretation of the results. Preoperative records were made the day before the procedure and its aims were carefully explained to the patient. All patients were in a modified Fowler's position (about one half) during the testing. Postoperative measurements were made on the first through the seventh postoperative days in the mid to late afternoon. Oxygen therapy was discontinued for at least one-half hour before the measurements were made. The patients in the first thoracotomy group had oximeter studies shortly after the forced vital capacity tracings, resulting in higher average oximeter readings than had been found in resting patients previously studied. In the second thoracotomy group, oximeter studies were not made until 5 to 10 minutes after the vital capacity measurements. Oximeter studies were also delayed 5 to 10 minutes in the control group.

RESULTS

Although there was considerable variation from patient to patient in all three patient groups, there was a striking tendency for the lowest values in any of the tests to be recorded on the second and third postoperative days in the two thoracotomy groups. Lowest values in the comparative group were recorded on the first postoperative day. The average values for each of the groups are tabulated in Tables II, III, and IV. It is obvious that patients undergoing thoracic surgery experience much greater alteration in pulmonary function than patients undergoing procedures far removed from the chest. It is also apparent that the impairment is of longer duration.

TABLE II. VITAL CAPACITY, OXYGEN SATURATION, TIMED VITAL CAPACITY, AND MAXIMUM EXPIRATORY FLOW AVERAGES FROM A GROUP OF 24 MALES UNDERGOING THORACIC SURGERY

TEST	PREOP.	POSTOPERATIVE DAY						
		1	2	3	4	5	6	7
Vital capacity								
Average (c.c.)	4,370	1,860	2,020	2,020	2,190	2,240	2,550	2,540
Average per cent of preop.	100.0	43.2	46.8	46.0	50.0	51.6	58.7	59.2
Per cent O_2 saturation	95.8	93.7	93.6	93.4	93.8	94.1	94.0	93.8
Timed vital capacity (%)								
1 second	71	67	66	65	66	67	63	64
2 second	85	84	81	82	82	83	81	80
3 second	90	92	89	90	90	90	87	87
Maximum expiratory flow (L./sec.)	6.5	2.1	2.3	2.3	2.3	2.5	2.7	3.0

Vital Capacity.—Vital capacities from day to day in the three groups are compared in Fig. 1. The vital capacity of patients undergoing thoracotomy decreased to an average of approximately one half of their preoperative volume. This was observed within the first 24 to 48 hours postoperatively in almost all

TABLE III. VITAL CAPACITY, OXYGEN SATURATION, TIMED VITAL CAPACITY, AND MAXIMUM EXPIRATORY FLOW AVERAGES FROM A GROUP OF 26 PATIENTS (BOTH SEXES) UNDERGOING THORACIC SURGERY WITH NEURECTOMY

TEST	PREOP	POSTOPERATIVE DAY 1	2	3	4	5	6	7
Vital capacity								
Average (c.c.)	2,700	1,440	1,425	1,475	1,520	1,520	1,595	1,625
Average per cent of preop	100.0	53.3	52.8	54.6	56.3	56.3	59.1	60.3
Per cent O_2 saturation	96.6	94.6	92.8	93.6	94.3	94.3	94.5	95.2
Timed vital capacity (%)								
1 second	70	75	77	76	75	75	74	73
2 second	87	90	88	89	87	88	88	87
3 second	93	94	94	92	92	93	93	93
Maximum expiratory flow (L./sec.)								
males	3.6	1.9	2.1	2.1	2.2	2.3	2.6	2.2
females	2.8	2.0	1.9	2.1	2.1	2.0	2.1	2.0

TABLE IV. VITAL CAPACITY, OXYGEN SATURATION, TIMED VITAL CAPACITY, AND MAXIMUM EXPIRATORY FLOW AVERAGES FROM A GROUP OF 25 PATIENTS (BOTH SEXES) UNDERGOING PERINEAL AND EXTREMITY PROCEDURES

TEST	PREOP	POSTOPERATIVE DAY 1	2	3	4	5	6	7
Vital capacity								
Average (c.c.)	2,960	2,580	2,810	2,890	2,840	2,740	2,590	2,720
Average per cent of preop	100.0	90.0	98.7	99.2	97.7	97.8	96.1	96.3
Per cent O_2 saturation	97.0	96.5	96.0	96.0	95.5	96.5	96.5	97.0
Timed vital capacity (%)								
1 second	73	78	76	75	77	73	77	76
2 second	88	91	90	88	90	89	90	88
3 second	94	96	94	93	95	94	94	93
Maximum expiratory flow (L./sec.)								
males	4.3	4.9	4.9	5.5	5.3	6.0	5.5	5.6
females	2.8	3.1	3.5	3.1	3.4	3.3	3.8	3.3

patients. Thereafter, there was a tendency for the vital capacity to rise slowly, so that, at the end of the first postoperative week, it averaged 60 per cent of the preoperative value. This rise is statistically significant ($P < 0.01$). There was no demonstrable difference between males and females in the second thoracotomy group, when the vital capacity was expressed as per cent of the preoperative value. There was not a sufficient number of patients to detect any difference between segmental resection and lobectomy, but patients undergoing pneumonectomy, plombage, or decortication experienced a greater fall in vital capacity than those undergoing lesser procedures. The addition of neurectomy to the surgical procedure did not affect the postoperative vital capacity significantly. But there was a tendency for this group to have a somewhat larger vital capacity for the first several postoperative days when compared to the non-neurectomy group.

By contrast, in the group of patients who did not have a thoracotomy, none experienced a decrease in vital capacity more than 50 per cent and the average fall was only 10 per cent. This occurred on the first postoperative day. On the second postoperative day, and thereafter, there was no significant difference from the preoperative average. The scatter in this group was large and some postoperative patients were found to have a vital capacity increased to 140 per cent of their preoperative capacity. A reasonable explanation of this is a combination of adaption to the testing technique and relief of anxiety following their successful surgery.

Timed Vital Capacity.—Timed vital capacity was measured at intervals of 1, 2, and 3 seconds and expressed as per cent of that day's vital capacity. Aside from the observation that the averages of all three groups were uniformly slightly below the accepted normal values, no significant change in timed vital capacity was noted. The daily averages of patients without thoracotomy at 1, 2, and 3 seconds were several per cent above those of the patients with thoracotomy, but the difference was not statistically significant. There was no significant sex difference.

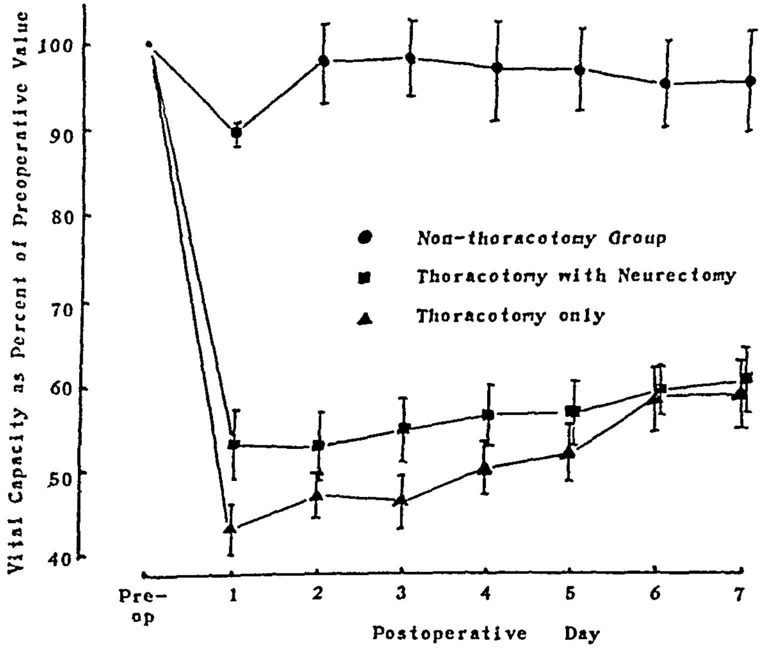

Fig. 1.—Vital capacity for 7 days postoperatively is plotted as the average of the daily per cent of preoperative vital capacity. For patients undergoing perineal and extremity procedures there is a slight decrease lasting only 1 day. There is a severe loss of vital capacity in those patients undergoing thoracotomy and pulmonary resection. There is no significant difference when intercostal neurectomy is added to thoracotomy. The vertical lines represent plus and minus one standard error of the mean.

Maximum Expiratory Flow Rate.—Since the timed vital capacity is a function of vital capacity and expiratory flow rate, and since both are severely reduced in the postoperative period, the maximum expiratory flow rate is a more objective measurement. It is well known that there is a marked sex difference in normal values of this measurement. This difference was found in both of our groups of mixed sexes. Fig. 2 shows the maximum expiratory flow rates of all three groups of patients with subdivision by sex in the appropriate groups. Following operation in the control group of patients, the expiratory flow rate shows an increase above the preoperative value This increase is believed due to both a learning process and satisfaction at a successful outcome of a minor operation In contrast, the maximum expiratory flow rate of thoracotomy patients was severely reduced in the first 24 to 48 hours Thereafter, there was a tendency toward improvement which, however, was of minimal degree Male and female both had similar absolute values in the range of 2.0 to 2.5 L per second This represents a greater per cent fall for the male, nearly 40 per cent, as opposed to 25 to 30 per cent for the female

Oximetry—In the control group there was no significant blood oxygen desaturation found postoperatively with the exception of 3 patients who had

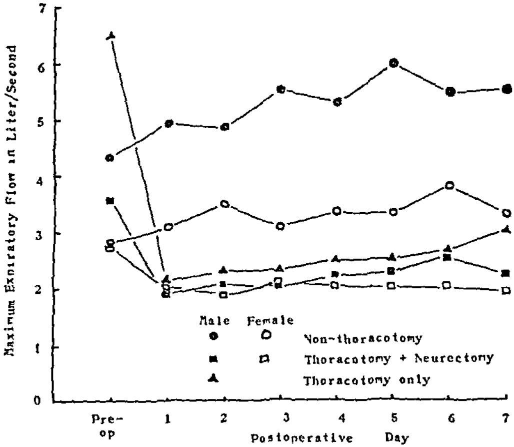

Fig 2—Daily maximum expiratory flow rates for 7 postoperative days is compared with preoperative values Patients undergoing perineal and extremity procedures show a slight day to day rise as they learn to perform the test better Patients undergoing thoracotomy suffer a marked fall with insignificant improvement in the first postoperative week

saturations of 87 to 90 per cent in the first 3 days These patients did not seem depressed clinically at this time and suffered no complications that could be associated with this desaturation The observed values may represent an error of the oximeter in these patients The average saturations of both thoracotomy groups fell significantly ($P < 0.05$) reaching a low of 2 to 3 per cent below preoperative saturation on the second and third days No sex difference was evident in the second group Since all of these measurements were made after two or more forced vital capacity determinations, they were expected to be somewhat higher than those found in the undisturbed patients Measurements in the first group of thoracotomy patients were obtained shortly after the vital capacity measurements and showed gradual day to day change This is consistent with previous observations[7] Since a different oximeter was used for the two thoracotomy groups, the tendency for the first thoracotomy group to be lower than the second probably represents a systematic error in the instrument. The changes in blood oxygen saturation found in the second thoracotomy group (which were recorded 5 to 10 minutes after the vital capacity measurements) showed a greater decrease in saturation with the lowest values being recorded on the second postoperative day. There was no significant change from day to day in the patients who did not have a thoracotomy and the saturations recorded were considered representative of the random scatter found with this instrument.

Clinical Observations.—Most patients in all three groups had quite benign postoperative courses as assessed clinically for their procedures. This is a reflection of modern surgical, anesthetic, and nursing techniques. There was a death in each of the thoracotomy groups. One patient, 15 days after a pneumonectomy, died in right-sided congestive heart failure. The other died 5 days following an Ivalon sponge plombage, with severe bronchopneumonia, congestive heart failure, and multiple pulmonary thromboses. Both were severely ill. Both had vital capacities below 30 per cent of their preoperative value, and both were clinically cyanotic. That both had a timed vital capacity of 60 per cent or more for the several days prior to death is merely a reflection of the evere reduction in lung volume. Maximum expiratory flow rate of both was ess than 0.9 L. per minute terminally, which is a markedly reduced value (normally 3 to 6 L. per minute for males).

Observations of respiratory rates showed a wide scatter from 4 per minute after a moderate overdose of Levo-Dromoran to 60 per minute terminally in a dying patient. Tachypnea was very frequent following the stir-up regime or taking of a chest roentgenogram. The respiratory rates recorded on the patient's chart by ward personnel (mostly aides) correlated best, however, with the numbers 18, 20, and 22. This phenomenon has been described in detail.[6] Pulse rates were somewhat more carefully observed and recorded and values found in the patient's chart were not far from values personally counted in several dozen spot comparisons. There was the usual diurnal variation. This was grossly modulated by pain relieving medication in one direction, and by stir-up procedures in the other. For illustrative purposes, the average envelopes of daily pulse rates are shown for the three groups in Fig. 3. The low values were usually recorded between the hours of 11 P.M. and 6 A.M., and the high values between 12 noon and 6 P.M. Both thoracotomy groups have been pooled for this figure.

Narcotic consumption in these three groups of patients is interesting. Narcotics were administered upon request of the patient, but potency and dosage were individually adjusted and regularly decreased after the second postoperative day. If possible, nothing stronger than codeine was given past the sixth or seventh postoperative day. In the thoracotomy group, maximum requirement (average 5.3 injections, usually 1 to 2 mg. of Dilaudid, per patient per day) was found on the second and third postoperative day, with reduction to three oral doses (usually 30 mg. of codeine) per patient per day by the second week.

In contrast, the maximum dosage in the control group was found on the first postoperative day (average 4.5 injections, usually 75 to 100 mg. of meperidine, per patient per day). On each of the next 2 days, the average number of doses per patient was halved. By the fifth postoperative day, only nine doses of codeine were administered to the entire group of 25 patients.

Complications.—There were eleven instances of nausea and emesis in the control group, eight of 2 days' duration, and one of 3 days' duration. In addition, there was 1 patient with acute pyelitis, 4 with undiagnosed temperature elevations, 1 with paralytic ileus, 1 with parotitis, and 1 who developed hypostatic pneumonia. With the exception of the patient with pneumonia, the saturations, expiratory flow rates, and vital capacities of these patients were not markedly abnormal.

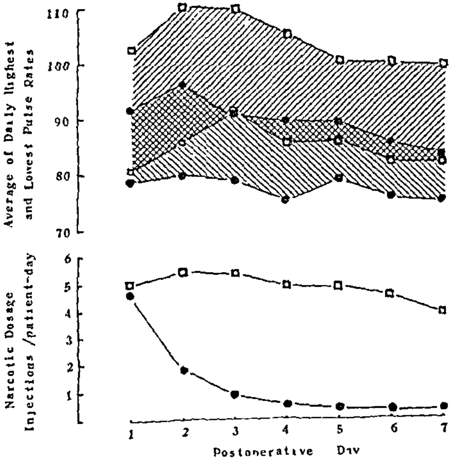

Fig 3.—*Upper graph*—Daily average of the highest and lowest pulse rates recorded for thoracotomy [illegible] compared with those of patients with perineal and extremity procedure [illegible] cant elevation for several days in the former group, but in [illegible] is greater in the thoracotomy patients and *Lower* [illegible] declines muc [illegible] ge were individually adjusted so as to relieve pain without [illegible]

Of the thoracotomy patients, there were 14 who developed major respiratory complications, including atelectasis, large hydropneumothorax, pneumonia, or empyema. There were eleven minor respiratory complications including patchy atelectasis, requiring no more than stir-ups to correct, or minor degrees of pneumohydrothorax. There was no nausea or vomiting of more than 4 hours' duration. There were no extrathoracic complications.

In general, these complications in all groups were of the expected nature and frequency for the procedure undergone.

DISCUSSION

The data here presented confirm previous reports of postoperative blood oxygen desaturation. They shed light on certain possible causes of hypoxemia and suggest further studies.

Timed vital capacity, as originally proposed, was intended to separate obstructive from restrictive pulmonary disease. If this interpretation is made of our results, it suggests that there is no gross obstruction imposed by thoracotomy. Gross changes in vital capacity as demonstrated are striking. Several patients were found to have vital capacities hardly greater than their tidal volumes. This underlines the importance of adequate re-inflation of lungs at the time of surgical closure and of prompt, vigorous treatment of atelectasis to provide as great a pulmonary reserve as possible. The late results of pulmonary resection have been shown frequently to be a small reduction in vital capacity. From this study, it is apparent that this capacity is only slowly achieved and for the first week or more respiratory reserve is dangerously small.

The maximum expiratory flow rate is perhaps the most interesting observation. This may be considered a test of the mechanics of breathing. When considered in correlation with the reduction of vital capacity, it shows that some patients subjected to thoracotomy must breath at or near their maximum breathing capacity. If there was no gross obstruction to air flow, as suggested by the timed vital capacity results, the reduction in flow rates must be due to a decreased force of expiration. Since narcotics may improve respiratory function in patients following surgery,[3] liberal but individualized narcotic dosage should be given. This point deserves further investigation.

Finally, it should be noted that the hemoglobin saturations recorded here are midway between the values before and after stir-up, as previously reported.[2] Since the blood oxygen saturation measurements were made from several minutes to 10-minute intervals after the two vital capacity efforts, it indicates the necessity of frequent stir-ups and the importance of patient cooperation in the postoperative nursing care if hypoxemia is to be fought adequately. Complacency is a danger well into the second postoperative week. Oxygen therapy should be considered for longer than the usual 6 to 24 hours.

There was no consistent tendency for the patients experiencing complications in our groups to have low values in any of the four measurements reported. Indeed, many patients with complications had normal or near normal saturations and greater vital capacity or expiratory flow rates than their group average. On the other hand, those patients who had low saturations (below 90 per cent), great reduction in vital capacity (below 40 per cent) or maximum expiratory flow rate below 1.5 L. per second, were at least twice as likely to develop complications.

The monograph, *Pulmonary Complications of Abdominal Surgery*, by Anscombe[7] provides comparable data on vital capacity and expiratory flow rates in a number of different abdominal operations. Only 2 cases are presented which involve thoracotomy, both trans-thoracic gastrectomy. In these there is no real improvement in vital capacity until after the third postoperative day.

By the eighth day the vital capacity reached the preoperative level On the first 3 days the vital capacity was about 50 per cent Maximum expiratory and inspiratory rates also remained severely low for the first 3 days In all of the other procedures studied, a total of 144 patients undergoing gastrectomy, cholecystectomy, nephrectomy, appendectomy, abdominal and inguinal herniorrhaphy, and bladder and prostate surgery, the nadir in the daily vital capacity and flow curves was exhibited on the first day and was followed by prompt improvement with essentially normal values by early in the second week Further, there was rarely more than a 40 per cent fall in vital capacity This indicates that there are marked quantitative differences in respiratory impairment following thoracotomy and laparotomy In either case the conclusion is reached that depressed respiratory function is a predisposing, although not necessarily causative, factor in the occurrence of complications Our previous report indicated that a decrease in pulmonary diffusing capacity for oxygen is not a prominent cause of hypoxemia This report presents evidence that hypoventilation is largely responsible This hypoventilation is a product of both reduction in lung volume and in the mechanical forces of breathing

Comparison of vital capacity and blood oxygen saturation before and after narcotic injection was made in several patients All showed improvement We feel that the frequent requests for narcotics and elevated pulse rates are evidence of pain which limits respiratory excursion and leads to hypoventilation This pain manifests itself in the decreased vital capacities and low expiratory flows When reaction to the surgical trauma is superimposed upon hypoventilation, the stage is set for pulmonary complications The attendant hypoxemia certainly interferes with normal function of the other systems of the body, especially in starting a vicious cycle of central nervous depression and further hypoventilation

We suggest that narcotic administration should be more liberal with greater attention to patient variation Addiction should not be considered a danger in the first postoperative week Careful patient instruction in the value and effects of the stir up regime is indicated preoperatively Oxygen therapy should be considered a prophylaxis and continued for several days with adequate humidification and mechanical assistors where necessary

SUMMARY

Observations of the day to day changes of vital capacity, oxygen saturation, timed vital capacity, and maximum expiratory flow rate in post thoracotomy patients are presented and compared with similar measurements made in a group of postoperative patients who had not had a thoracotomy Marked reduction in volume and expiratory flow rate was found with insignificant improvement in the first 3 postoperative days, during which blood oxygen saturation is lowest During this 3 day period, clinical signs and narcotic demand suggest painful respiration which promotes hypoventilation The addition of neurectomy to the surgical procedure does not alter significantly the immediate postoperative changes in vital capacity, timed vital capacity, or

maximum expiratory flow rate, but a slight benefit is suggested. Increased use of the stir-up regime, more liberal narcotics for pain control, and more frequent use of prolonged oxygen therapy seem warranted.

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LEFT VENTRICULAR FUNCTION FOLLOWING ELECTIVE CARDIAC ARREST

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ACUTE heart failure is occasionally observed following a period of elective cardiac arrest induced in the course of an intracardiac operation employing cardiopulmonary bypass This complication, with its attendant increase in operative mortality was encountered in this clinic in patients without severe pulmonary hypertension or other lesions predisposing to failure and suggested that arrest itself might have a depressant effect on myocardial contractility

In order to evaluate the effects of arrest and of arresting agents on the heart changes in myocardial contractility were measured Left ventricular function curves were utilized in the study for this purpose and were established in normal dogs before and following cardiopulmonary bypass and arrest induced by various techniques A ventricular function curve expresses the stroke work of the ventricle over a wide range of filling pressures and permits assessment of its contractility at increasing degrees of stress[1]

METHODS

The experimental method described by Sarnoff and Berglund[1] was modified to permit its application with extracorporeal circulation Healthy mongrel dogs weighing 11 5 to 22 5 kilograms were employed The animals were anesthetized with intravenous thiopental and ventilation was maintained by a mechanical positive pressure respirator The cannulations and extracorporeal circuit are illustrated in Fig 1 The right chest was opened through the fifth intercostal space The venae cavae were exposed, the right pulmonary artery and azygos vein were dissected free, and the pericardium was widely incised Heparin (3 mg per kilogram) was given intravenously and the previously exposed femoral artery was cannulated The right atrium was cannulated through the azygos vein The right pulmonary artery was occluded distally and a thin walled stainless steel cannula was placed into the proximal end A right pulmonary vein was cannulated for measurement of left atrial pressure Large

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polyvinyl catheters were placed in the superior and inferior venae cavae through the right atrial appendage. The extracorporeal circuit was completed with a rotating disc oxygenator[2] with a single arm nonocclusive roller pump. Venous blood from the venae cavae was drained by gravity into a reservoir. To decompress the heart, intracardiac blood was drained from the right atrium through the azygos vein into a reservoir which in turn emptied into the main venous reservoir. The temperature of the animals was maintained at normal levels by warming coils on the oxygenator. The pump-oxygenator was primed with blood obtained from donor dogs which had been lightly anesthetized with thiopental. The partial pressure of the oxygen in the blood at the arterial end of the oxygenator was monitored by a Clark oxygen electrode[3]; 99 per cent oxygen and 1 per cent carbon dioxide were added to the oxygenator at a rate equal to systemic arterial flow. Aortic and left atrial pressures were measured by Statham pressure transducers and recorded together with the electrocardiogram on a multichannel direct-writing oscillograph.

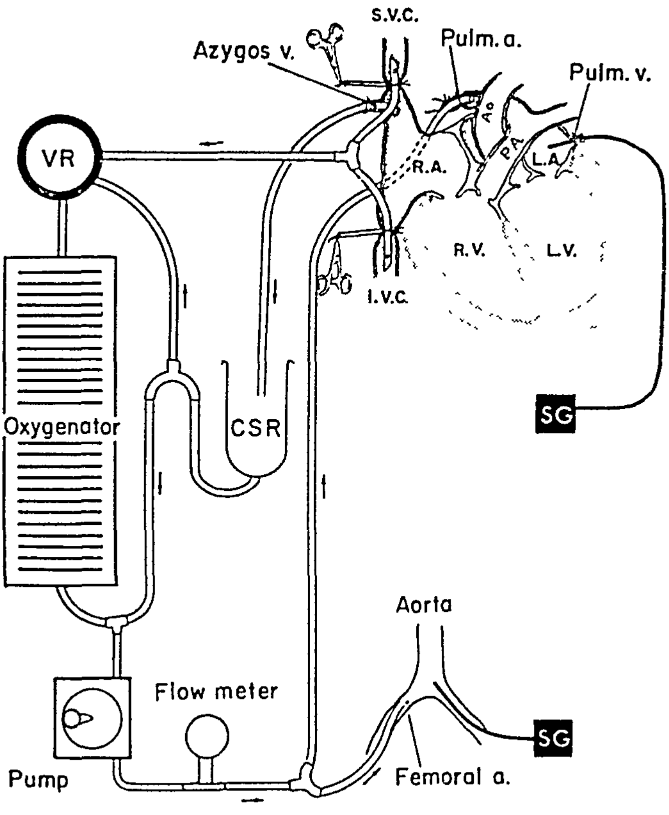

Fig. 1.—Diagrammatic representation of the experimental method employed to assess ventricular function and provide complete cardiopulmonary bypass. *CSR*—right atrial drainage reservoir; *VR*—venous reservoir; *SG*—Statham pressure transducer. In establishing ventricular function curves the venous return bypassed the oxygenator and was returned to the pulmonary artery through the electromagnetic flowmeter. During complete bypass the venous blood was oxygenated and returned through the meter to the femoral artery.

When the left ventricular function curves were inscribed, venous blood did not enter the oxygenator but was pumped through a buffer bottle and the cannula of an electromagnetic flowmeter[4] and into the right main pulmonary artery. Prior to arrest, a control function curve was obtained by measuring left atrial pressure and central aortic pressure as the flow into the pulmonary artery and hence left ventricular output (less coronary flow) was increased in a stepwise fashion Each period of observation lasted 2 minutes allowing for stabilization of all parameters and established one point on the curve The function curve was terminated when the mean left atrial pressure exceeded 26 cm water or systemic flow exceeded 150 ml per kilogram per minute

Complete cardiopulmonary bypass was then initiated by directing the venous return through the oxygenator and returning it to the femoral artery Systemic flow was maintained at 100 ml per kilogram per minute Two to 3 minutes after the initiation of bypass the ascending aorta was cross clamped above the coronary ostia Acetylcholine arrest was initiated by the injection of 15 mg per kilogram of body weight of the drug, diluted in saline, into the ascending aorta below the clamp[5] Arrest with potassium citrate was carried out by rapidly injecting a 2 5 per cent solution of potassium citrate in whole blood into the ascending aorta until the heart stopped The technique was that described by Melrose[6] Anoxic arrest was induced by aortic occlusion alone With all forms of arrest, the right atrium was vented by the cannula in the azygos vein The lungs were not ventilated during bypass Periods of arrest were 10, 20, and 30 minutes During "intermittent" anoxic arrest, the ascending aorta was clamped for 4 minutes and released for 1 minute of each 5 minute period

At the end of arrest total cardiopulmonary bypass was continued for approximately 10 minutes until adequate heart action was restored When potassium citrate had been employed 1 or 2 ml of 10 per cent calcium chloride was injected directly into the left ventricle to inhibit the effects of the potassium ion Following acetylcholine arrest, 0 4 mg atropine sulfate solution was injected into the circulation to neutralize the effects of this arresting agent If obvious severe failure persisted, 1 or 2 ml of epinephrine (1 10,000) was injected into the left ventricle Twenty minutes after termination of arrest a second ventricular function curve was obtained in a manner similar to that just described In 2 dogs, left ventricular function curves were obtained before and after 20 minutes of total cardiopulmonary bypass without elective cardiac arrest

Left ventricular function was determined by relating left ventricular stroke work to mean left atrial pressure The former parameter was derived from the equation

$$\frac{LVS = (Ap - LAp) \times SV}{100}$$

Where

LVS = left ventricular stroke work gram meters
Ap mean aortic pressure (cm water)
LAp mean left atrial pressure (cm water)
SV stroke volume $= \frac{\text{systemic flow (ml /min)}}{\text{heart rate}}$

The effect of the arresting agent was determined by a comparison of the control and post arrest curves in each experiment In each instance the post arrest curve could be described as showing minimal or no depression, moderate depression, or severe depression of myocardial contractility. Pairs of function curves illustrative of these classifications are shown in Figs. 2, 3, and 4. Some animals exhibited such severe depression that no function curve could be obtained following arrest.

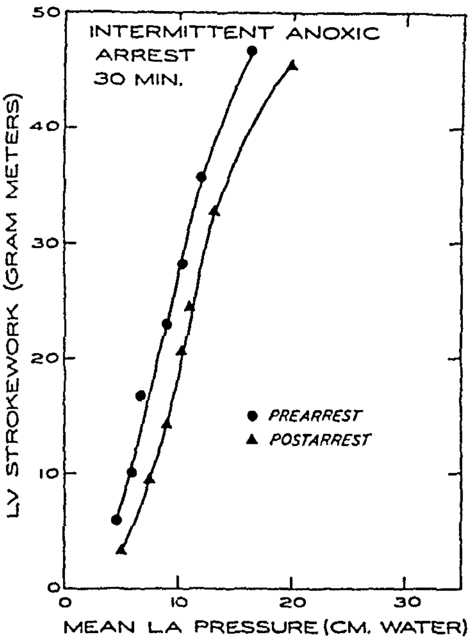

Fig. 2.—Left ventricular function curves before and after intermittent aortic occlusion for 30 minutes. This pair of curves is illustrative of minimal or no depression of left ventricular function.

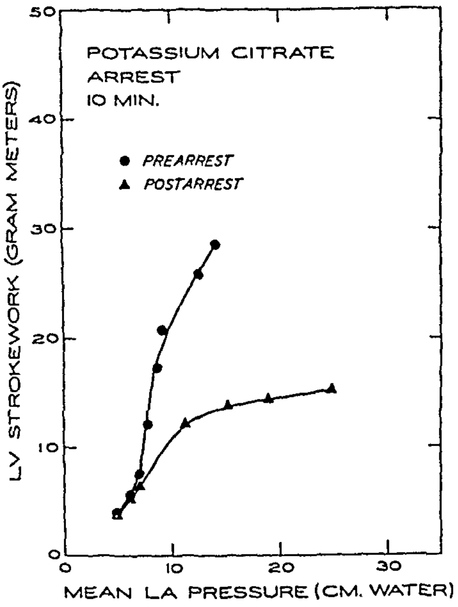

Fig. 3.—Left ventricular function curves before and after elective cardiac arrest for 10 minutes with potassium citrate administered by the Melrose technique. This pair of curves is illustrative of moderate depression of left ventricular function.

RESULTS

The effects of cardiac arrest on left ventricular function were studied in 44 dogs. The results of the studies are summarized in Table I. In the 2 animals studied before and after bypass, but without cardiac arrest, left ventricular function curves were unchanged by the perfusion. When potassium citrate was employed (15 animals), complete arrest always resulted and the heart evidenced no mechanical or electrical activity. However, restoration of normal contraction was difficult and intracardiac epinephrine was at times necessary before an effective beat could be established. In 5 of the 15 animals, myocardial depression was so severe that no post arrest function curve could be

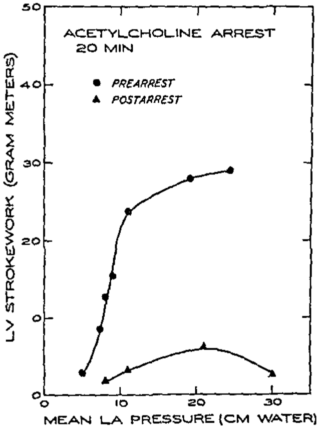

Fig. 4.—Left ventricular function curves before and after elective cardiac arrest for 20 minutes with acetylcholine. This pair of curves is illustrative of severe depression of left ventricular function.

Table I. The Effects of Various Forms of Cardiac Arrest on Left Ventricular Function

TIME	AGENT	NUMBER OF DOGS AND DEGREE OF MYOCARDIAL DEPRESSION (SEE TEXT): MINIMAL OR NONE	MODERATE	SEVERE	NO POST ARREST VF CURVE OBTAINABLE	TOTALS
10 min	Potassium citrate	3	3		2	8
	Acetylcholine	5	1			6
	Anoxia	3	2	1		6
20 min	Potassium citrate	1			3	4
	Acetylcholine			2	2	4
	Anoxia	2	1	2		5
30 min	Potassium citrate			3		3
	Acetylcholine	1		1	1	3
	Anoxia (intermittent)	4	1			5

obtained. With 20 and 30 minutes of arrest, 6 of 7 dogs revealed severe depression when potassium citrate was employed. At 10 minutes, 2 of 8 hearts were unable to sustain the systemic circulation but 3 showed minimal or no depression and 3 showed only moderate depression.

Thirteen dogs underwent cardiac arrest with acetylcholine. When the agent was injected into the ascending aorta the heart usually stopped for 2 minutes and then resumed a beat at a slow rate. At the end of arrest, especially in those animals in the 20- and 30-minute groups, ventricular fibrillation frequently occurred, but in general was readily reversed by electrical shock after coronary perfusion had been restored and atropine administered. However, in 3 animals, depression was so severe that no post-arrest function curve was obtainable. When arrest with acetylcholine was employed for only 10 minutes, 5 of 6 animals had minimal or no depression and 1 showed moderate depression.

Sixteen dogs were subjected to arrest induced by anoxia. After the ascending aorta was clamped, the heart usually continued to beat for approximately 5 minutes but with gradually decreasing vigor until mechanical activity ceased. Ventricular fibrillation was not uncommon but was readily converted to a sinus mechanism by shock and the restoration of coronary perfusion. Normal sinus rhythm was re-established in all 16 animals. After 10 minutes of arrest, 3 dogs showed minimal or no depression, 2 showed moderate depression and 1 had severe depression of function. After 20 minutes of anoxia, 2 dogs showed minimal impairment of function, 1 moderate and 2 severe depression.

When the aorta was intermittently occluded for 30 minutes, only 1 of 5 dogs exhibited any significant depression of ventricular function and in this animal it was of only moderate severity.

DISCUSSION

The experimental study described was suggested by the clear evidences of left ventricular failure which were observed in a number of patients in whom potassium citrate arrest was employed as an adjunct to cardiopulmonary bypass. The value of ventricular function curves as effective indicators of changes in contractility is apparent from a comparison of the pre- and post-arrest curves reproduced in Figs. 3 and 4. When the ventricle is performing little work, depression of function may not be apparent since filling pressure may remain low. When, however, the heart must deal with a greater work load it may be able to do so only with a greatly increased filling pressure, if at all.

The majority of patients operated upon for heart disease have an increased myocardial work load and although a successful correction of the anatomic lesion may substantially reduce this, the trauma of the operative procedure may offset this beneficial effect in the early postoperative period. It has been shown, for example, that right ventriculotomy alone impairs ventricular function.[7] Thus the additional depression of ventricular function caused by cardiac arrest may be sufficient to result in fatal heart failure.

The ventricular function curves in the present study were established by modification of the methods described by Sarnoff and Berglund[1] and Stirling and his associates[7] Although the measurements of systemic flow did not include the coronary flow, the magnitude of the latter has been shown to be too small to be of significance in such experiments[1] The heart rate was not maintained constant during the studies, even though the rate can influence ventricular function[8] However, it was considered that the conditions of the study paralleled the clinical situations in which arrest is employed and rate is not controlled Decompression of the heart during the arrest and recovery periods has been shown to be an important adjunct to the technique[9] and the adequacy of drainage was shown by the fact that the mean left atrial pressure remained low during arrest

In the present study the methods of cardiac arrest most often employed clinically were evaluated Potassium citrate was uniformly responsible for severe depression of function after 20 and 30 minutes of arrest Even at 10 minutes, 2 of 8 dogs could not maintain a heartbeat Calcium chloride was injected into the left ventricle to inhibit the effects of the potassium ion, since it is known that these two ions have a directly antagonistic action However, epinephrine was at times required for the hearts to resume any function and they were often observed to be flabby and weak These findings in regard to potassium citrate arrest are in contrast to those of Darby and co workers[10] who did not observe depression of contractility when the effects of potassium were assessed with the Walton Brodie strain gauge arch The latter method, however, measures the function of only an isolated ventricular segment and Gilbert[11] has shown that the distribution of the arresting agent is not necessarily uniform Both clinical[12] and experimental studies[13] have demonstrated that the infusion of potassium citrate into the coronary bed may produce myocardial necrosis and it is suggested that this anatomic lesion is responsible for the physiologic sequelae noted

The hearts arrested with acetylcholine evidenced virtually no impairment of function when the period of arrest was 10 minutes However, with longer periods of arrest the function curves were as severely depressed as with potassium citrate These hearts, in contrast to those arrested with potassium, always resumed a beat, sometimes after a period of ventricular fibrillation, and epinephrine was seldom necessary As noted above, the period of complete arrest with acetylcholine seldom lasted more than 2 minutes but the slow beat which ensued would certainly not hamper the performance of an intracardiac procedure

Uninterrupted aortic occlusion leading to anoxic cardiac arrest apparently resulted in less impairment of ventricular function than either potassium citrate or acetylcholine at 20 minutes The data do not clearly show an advantage of anoxia over acetylcholine at this time but it was not considered that further experiments to establish this point were necessary Severe depression was observed in only 3 of the total of 11 dogs in which the effects of anoxia were studied for 10 or 20 minutes and in every instance the function of the heart was good enough to permit the curves to be established after the arrest period When the aorta was clamped intermittently for 30 minutes ventricular function was virtually unchanged The heart, under these circumstances, never evidenced complete lack of contraction but, as with acetylcholine, the slow beat which continued would not have interfered with a surgical procedure. In these animals epinephrine was never necessary in the post-arrest period.

Pairs of ventricular function curves cannot be related by any simple mathematical index and it is apparent that the results of the experiments described do not lend themselves to quantitative analysis. The evidence seems abundant, however, from the marked qualitative differences in the curves, that cardiac arrest induced for more than 10 minutes with either potassium citrate or acetylcholine is almost uniformly associated with subsequent severe depression of myocardial function. These physiologic observations and the histologic observation of myocardial necrosis in the hearts of patients dying after potassium arrest[12] have led to the abandonment of this technique at the National Heart Institute in clinical practice. Intermittent aortic occlusion has proved the most satisfactory method for securing a dry and quiet field. It cannot be employed, however, in operations requiring aortotomy for extended periods and direct selective coronary perfusion has been found the technique of choice under these circumstances.

SUMMARY

Myocardial contractility, as measured by left ventricular function curves, was studied in normal dogs before and after periods of cardiac arrest induced with either potassium citrate, acetylcholine, or anoxia (continuous or intermittent). Both potassium citrate and acetylcholine resulted in severe depression of myocardial function when the period of arrest exceeded 10 minutes. Continuous aortic occlusion for 10 or 20 minutes was responsible for only moderate impairment of function and intermittent aortic occlusion caused no significant depression when continued for 30 minutes. The results of the studies suggest that intermittent aortic occlusion, without the infusion of cardioplegic agents, is the technique of choice for open cardiac operations not necessitating prolonged aortotomy.

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THE MECHANISM AND PREVENTION OF AIR EMBOLISM DURING CORRECTION OF CONGENITAL CLEFT MITRAL VALVE

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During open-heart surgery the prevention of air entrapment and subsequent embolization from the operative field may be difficult under certain conditions. The occurrence of two instances of fatal air embolism in a series of 7 patients with congenital cleft mitral valve, during a period in which 70 open-heart procedures were performed for other defects at this institution with no deaths due to this cause, prompted a study of the mechanism and prevention of this complication in the correction of this particular defect.

The problem of air embolism during the open correction of acquired mitral disease has been noted by many authors.[1, 8] Air can be trapped in the left ventricle and, with the patient in the left lateral decubitus position, the right pulmonary veins may be an additional source of trapped air. The excellent studies of Kay and associates[3] have demonstrated that embolization from the left ventricle occurs only when left ventricular pressure is sufficiently great to open the aortic valve. This can be prevented in the dog by keeping the mitral valve incompetent until the left heart is completely filled with blood. Gott and associates[2] have described the use of a spring-like instrument called the mitral spiral to achieve this end.

Pertinent data concerning 7 patients undergoing closure of partial or complete cushion defects involving repair of congenital cleft mitral valve are presented in Table I.

The diagnosis of cleft mitral valve with persistent ostium primum or atrioventricularis communis was suggested preoperatively in all patients by the demonstration of left-to-right shunting at the atrial level associated with a systolic thrill and characteristic electrocardiographic findings. All patients had left axis deviation, horizontal heart, and right ventricular hypertrophy or incomplete right bundle branch block. Three had prolongation of the P-R interval.

All patients were operated upon in the supine position; 6 had a median sternotomy. Perfusion was satisfactory in all respects and followed the principles outlined in a previous publication from this clinic.[10] At operation, 4

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TABLE I AIR EMBOLISM DURING CORRECTION OF CONGENITAL CLEFT MITRAL VALVE

NUMBER	AGE	PATHOLOGY	LEFT VENTRICULAR CATHETER	MITRAL SPIRAL	AIR EMBOLUS	RESULT	COMMENT
1	6	Persistent ostium primum Cleft mitral valve Cleft tricuspid valve	No	No	No	Died	Death due to respiratory insufficiency
2	5	Persistent ostium primum Cleft mitral valve	No	No	Yes	Died	Death due to air embolism
3	7	Persistent ostium primum Cleft mitral valve	Yes	No	No	Alive	
4	11	Persistent ostium primum Cleft mitral valve	Yes	No	No	Alive	
5	6	Persistent ostium primum Cleft mitral valve	Yes via atrial septum	No	No	Alive	
6	7	Persistent atrioventricular canal	No	Yes	Yes	Died	Death due to air embolism
7	17	Persistent atrioventricular canal	Yes	Yes	No	Alive	

patients were found to have partial cushion defects with a typical ostium primum atrial septal defect and cleft mitral valve. One had a cleft tricuspid valve in addition. Two patients were found to have a complete cushion defect or persistent atrioventricular canal. The technique of correction was similar to that described by others[7] and consisted of closure of the mitral and tricuspid clefts with interrupted fine silk, in some instances tied over a strip of Ivalon sponge. The associated septal defect was closed with a compressed Ivalon prothesis. Cardiac arrest was not used. In all patients, except Patient 3 who had a persistent murmur of mitral insufficiency postoperatively, a satisfactory repair was noted at the time of operation and confirmed by clinical course or autopsy.

There were three deaths in this series. The first patient and the only one to have a bilateral thoracotomy died of respiratory insufficiency after regaining consciousness with no neurological sequelae. The other two deaths were due to severe brain damage.

AIR EMBOLISM

Precautions to avoid air embolism were taken in the first 2 patients by allowing the left heart to fill with blood prior to complete closure of the atrial septal defect. While this was effective in Patient 1, Patient 2 died 36 hours following surgery of overwhelming brain damage without regaining consciousness. During bypass there was slowing and flattening of the electroencephalograph despite a satisfactory perfusion with respect to arterial and venous pressures and blood gas studies. Autopsy revealed complete correction of the defect and no obvious cause of death. The brain appeared normal by gross and microscopic examination.

As noted in Table I, special care was taken to avoid the trapping of air in the left ventricle in the remaining 5 patients and was successful except in Patient 6 who died 4 days postoperatively without regaining consciousness. Care was taken in this patient to fill the left heart prior to complete closure of the atrial septal defect and to keep the mitral valve incompetent by means of the mitral spiral. Autopsy revealed excellent correction of the cardiac defect and small fresh hemorrhages in the leptomeninges and cerebral substance generally (Fig. 1). These were confirmed on microscopic examination.

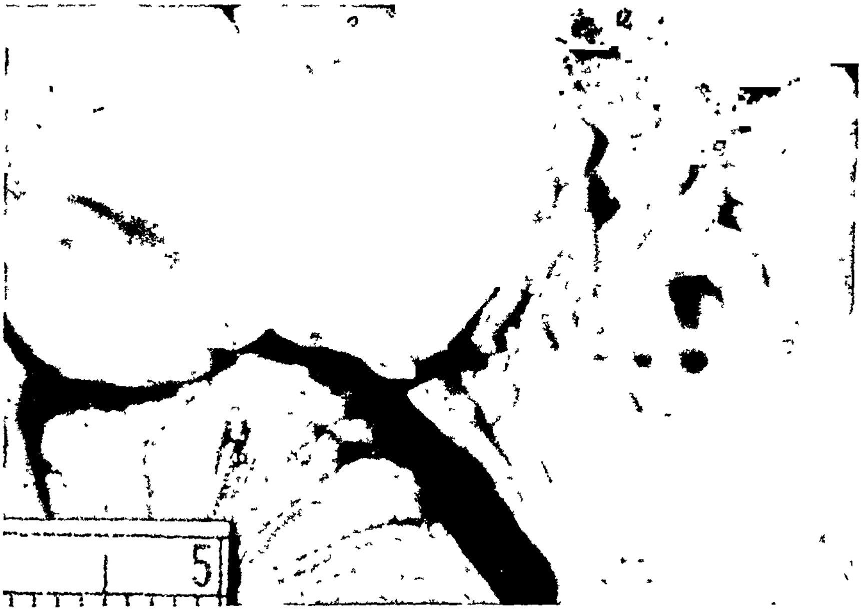

Fig. 1.—The cut surface of the brain of Patient 6 demonstrates numerous hemorrhagic areas

The occurrence of fatal brain damage in 2 patients of this series, despite the exercise of reasonable caution with Patient 2 and the use of the mitral spiral in Patient 6, prompts a review of the possible mechanism of air embolism under these circumstances.

While correction of acquired mitral disease is best carried out via a right anterolateral or lateral thoracotomy, the patients in this series were operated upon in the supine position via a median sternotomy or bilateral thoracotomy. This enables a complete exploration for patent ductus arteriosus, left superior vena cava and other congenital defects that cannot always be ruled out by cardiac catheterization and other means prior to surgery. The advantages of the median sternotomy in the correction of congenital cardiac defects have been listed by Lillehei and others.[6]

Fig. 2 demonstrates the relationship of the left ventricle to the left and right atrium in the supine position. Air introduced into the left ventricle during mitral valve correction via the atrial septal defect will rise to the apex of this chamber and may not be easily removed except by aspiration through the apex itself. Maintenance of mitral insufficiency until left heart closure is complete may still allow air to remain in this high pocket. As left ventricular ejection becomes effective this will be expelled into the aorta. Under these circumstances only one cubic centimeter of air per kilogram of body weight is necessary in the dog to cause significant brain damage and death.[5] The failure of maintenance of mitral insufficiency to prevent air embolism following mitral surgery for congenital cleft in Patient 6 and the success of this method when the right lateral or anterolateral approach is used for acquired mitral disease is probably explained by the dependent position of the apex of the heart during the latter approach.

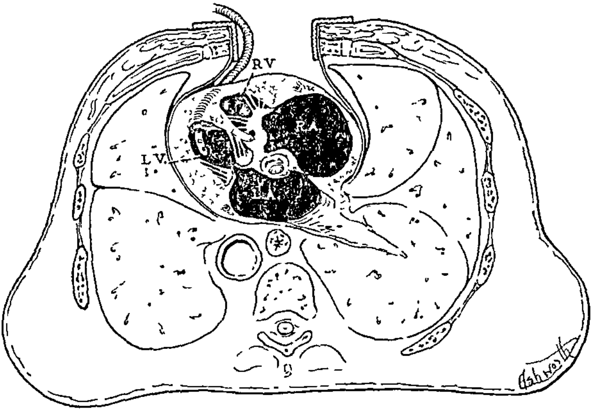

Fig 2 —This transverse section of the trunk at the level of the mitral valve demonstrates the relationship of the left ventricle with regard to other chambers in the supine position with a midline sternal-splitting approach Air introduced into the left ventricle is removed by a left ventricular catheter

PREVENTION

A reasonable approach to the prevention of air embolism following repair of a cleft mitral valve in the supine position would appear, therefore, to be the use of a left ventricular catheter as a vent. While on suction this will prevent left ventricular pressure from opening the aortic valve and, prior to its removal, air can be removed from the apex. Thus, with the patient in the supine position the heart is approached by a midline sternal-splitting incision with arterial cannulation via the common femoral artery. The patient is then placed on cardiopulmonary bypass and, following adequate decompression of the heart, it is gently lifted from its bed as seen in Fig. 3. A small stab incision is made in an avascular area of the apex extending part way but not completely through the myocardium. A 22 or 24 Fr. plastic cardiovascular catheter with multiple side perforations is passed into the left ventricle and held in position by a purse-string suture. The heart is then allowed to drop back into the pericardium as in Fig. 4 and the catheter is connected to the coronary suction circuit. The catheter is momentarily clamped to allow left heart filling following mitral repair while the valve is rendered incompetent by a suitable instrument and the atrial septal defect is closed. The mitral spiral has proved most satisfactory for this purpose. As soon as the left heart is closed the catheter is unclamped and the mitral spiral removed. The apex is now gently elevated and the catheter disconnected from the suction circuit and slowly removed while open to the atmosphere. One is quite surprised by the quantity of air expelled during this maneuver. The small stab incision will require one or two sutures for hemostasis and the heart is allowed to fall back into the pericardium. The patient is then taken off cardiopulmonary bypass and decannulation is effected in the usual way.

The use of the left ventricular apical catheter alone was most satisfactory in Patients 3 and 4. In Patient 5 no difficulty was encountered when the mitral valve was kept incompetent by means of a catheter passed through the atrial septal defect and left in place until the atrial septum was almost completely closed. This led to the use of the mitral spiral alone in Patient 6 with disasterous consequences. Catheter decompression was reinstituted with Patient 7 and a large quantity of air was obtained from the catheter just prior to its removal.

DISCUSSION

It is of significance that two of the three deaths in this series resulted from brain damage and, in both of these, catheter decompression was not used. While it is difficult to be certain that air embolus was the actual cause of these two fatalities, the satisfactory bypass in all other respects and the appearance of air in the left ventricular catheter in those cases in which it was used suggest that these deaths were indeed due to air embolus from the operative field.

The use of a left ventricular vent as a means of avoiding air embolism was suggested by Miller and associates[6] in the repair of ventricular septal defects in dogs. This has not been found necessary in the human being since the defect is usually in a superior position in relation to the left ventricular chamber and if reasonable caution is exercised to fill the left ventricle with blood prior to complete closure, air will not be trapped in this chamber. The suggestion by Kunkler and his associates[5] that the operative field be flooded with carbon dioxide has not gained widespread acceptance. A prophylactic method based upon a knowledge of the mechanism by which air trapping occurs is more likely to be uniformly successful.

The use of a left ventricular decompressing catheter in operation upon the mitral valve in the supine position fulfills this criterion and is suggested by the results in this series of patients. This will allow continued use of the median sternotomy and the supine position for correction of this defect.

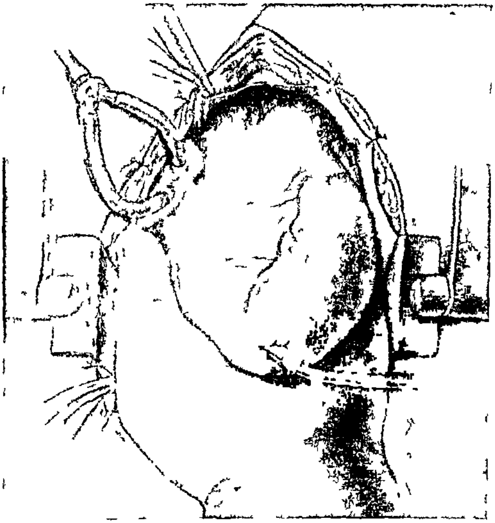

Fig 3 —This drawing demonstrates the ease of insertion of the left ventricular apical catheter following cardiac decompression at the start of cardiopulmonary bypass

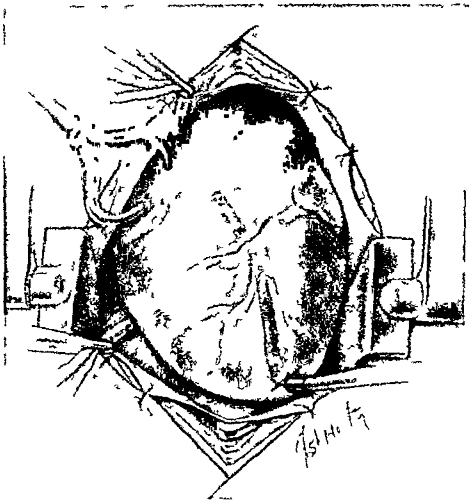

Fig 4 —This drawing demonstrates the catheter in place with the heart dropped back into the pericardium

SUMMARY

The problem of air embolism occurring in 2 of 7 patients with cleft mitral valve operated upon in the supine position is reviewed. The importance of air entrapment in the apical portion of the left ventricle as a source of this complication is noted and a means of prevention by left ventricular catheter decompression is suggested. This has proved to be a simple and effective means of avoiding air embolism in those instances in which it has been used.

ADDENDUM

Since submission of this paper, 3 additional patients with congenital cleft mitral valves have been operated upon with an excellent clinical result and no evidence of air embolism. Two had an ostium primum atrial septal defect associated with cleft mitral valve and were operated upon through a right anterolateral approach. Since the apex of the left ventricle is dependent with the patient in this position, a mitral spiral alone was used. The third patient had a complete atrial ventricular canal and since the supine position was used with a sternum-splitting incision, both the mitral spiral and left ventricular decompression were used.

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THE ROLE OF EPINEPHRINE AND NOREPINEPHRINE IN REBOUND CARDIOVASCULAR PHENOMENA IN AZYGOS FLOW STUDIES AND CARDIOPULMONARY BYPASS IN DOGS

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STEWART and Rogoff[15] first reported that substantial increments in arterial blood pressure were obtained when the venae cavae were released after a brief period of complete occlusion. It was later observed by Walton and his associates[16] that a similar increase in cardiac contractile force could be demonstrated in this way. Other investigators have demonstrated marked changes in cardiovascular functions following periods of acute severe anoxia[19, 20] or hypercapnia.[1] The increase or rebound has also been frequently observed during studies of "azygos flow" and of experimental cardiopulmonary bypass with low flow rates.[10] It is the purpose of this paper to report on the plasma levels of epinephrine and norepinephrine in dogs during and following azygos flow studies and cardiopulmonary bypass at various flow rates.

METHODS

The mongrel dogs used in these experiments were anesthetized with intravenous pentobarbital (30 mg. per kilogram) and respired on room air with an intermittent positive pressure mechanical respirator. Simultaneous recordings of arterial blood pressure, myocardial contractile force, and a standard lead of the electrocardiogram were made continuously. A Statham transducer attached to a femoral arterial cannula was used to monitor the blood pressure, and myocardial contractile force was measured by the use of a strain gauge arch sutured to the surface of the right ventricle. A description of the strain gauge arch[2] and the relationship of contractile force to other cardiovascular events have been reported.[4, 5, 6] All recordings were made by the use of Sanborn or Brush multichannel recording devices. A right intercostal thoracotomy incision in the fourth interspace was used in all cases.

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The experiments were divided into two groups. The first group, consisting of 11 dogs, was subjected to azygos flow studies. Umbilical tape ligatures were placed around the superior vena cava distal to the azygos vein and around the inferior vena cava, following the methods outlined by Cohen and Lillehei.[3]

The second group, consisting of 8 dogs, was subjected to a cardiopulmonary bypass. The right auricular appendage was the site of insertion of two polyvinyl plastic cannulae, one of which was advanced into each vena cava. The right femoral artery was cannulated for the return of oxygenated blood. A DeWall type oxygenator, in conjunction with a Sigmamotor pump apparatus, was used during the bypass.

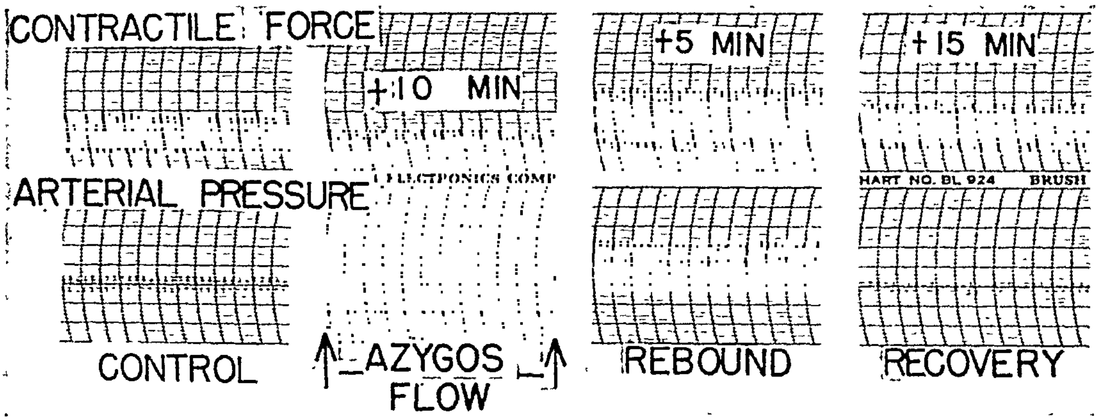

Fig. 1.—Effects of azygos flow on myocardial contractile force and blood pressure. See discussion in text.

Blood samples for the determination of the catechol amine levels were obtained from a cannula inserted into the opposite femoral artery. The samples were drawn in the following order: (1) initial control level; (2) just prior to the termination of azygos flow or cardiopulmonary bypass; (3) at the time of maximum increase in blood pressure and contractile force (if there was any increase); and (4) at the time of the return of contractile force to near normal levels.

The plasma concentrations of epinephrine and norepinephrine were assayed using the fluorimetric method of Weil-Malherbe and Bone,[17] as modified by Richardson and his co-workers.[13] This type of measurement and its clinical significance have been comprehensively reviewed by Manger and his associates.[13a]

RESULTS

In 8 of the 11 dogs in the first group, occlusion of the venae cavae for periods of 7 to 10 minutes resulted in a rapid decline in myocardial contractile force. This was followed by a gradual return of the contractile force toward normal during the course of the continued venous occlusion. Release of the venae cavae after 7 to 10 minutes of occlusion was followed by an increase in contractility and blood pressure, generally in the range of 40 to 50 per cent above control levels. The maximum increment in contractile force and blood pressure occurred at approximately 2 to 5 minutes after normal flow was reinstated. Fig. 1 shows a recording of myocardial contractile force and blood pressure changes typical of those obtained in 7 dogs during and immediately after the period of caval occlusion. Plasma levels of catechol amines were measured in 6 dogs. As shown in Table I, the total catechol amine levels increased markedly during the period of decreased blood flow from a mean control level of 3.0 to 91.8 micrograms per liter of plasma. In all experiments the major increment was in the epinephrine fraction although substantial increases in norepinephrine were obtained in 5 animals. Following the release of the vena cava, catechol amines returned toward control levels. At the time of the maximum rebound increase in cardiac contractile force epinephrine and norepinephrine levels were still elevated but were less so than during the period of reduced flow. Approximately 15 minutes following release of the occlusion catechol amine concentrations and contractile force had returned to near control levels.

TABLE I. PLASMA CATECHOL AMINES DURING PERIODS OF AZYGOS FLOW AND CARDIOPULMONARY BYPASS

	CATECHOL AMINES (MICROGRAMS PER LITER OF PLASMA)							
	CONTROL		DURING ALTERED FLOW		REBOUND		RECOVERY	
	E*	NE†	E	NE	E	NE	E	NE
Azygos Flow								
1	0.1	1.2	51.4	60.1	6.0	11.2	3.6	8.8
2	0.1	1.8	111.0	52.0	117.0	32.5	‡	‡
3	0.0	2.1	57.6	17.5	11.2	5.2	0.4	4.0
4	1.9	3.9	60.0	12.4	17.6	5.7	0.1	4.7
5	0.3	2.7	40.0	4.7	14.7	2.6	‡	‡
6	1.9	2.5	56.5	18.7	‡	‡	2.3	2.7
Mean	0.7	2.3	64.2	27.6	33.3	11.4	1.6	5.1
Cardiopulmonary Bypass								
20 c.c./Kg./min.								
1	0.5	2.3	10.9	6.1	6.5	5.2	0.7	4.8
2	0.1	2.7	59.0	53.0	5.9	11.5	4.0	7.9
3	4.1	3.7	105.9	37.0	‡	‡	‡	‡
4	0.4	2.0	66.2	7.0	402.7§	117.0§	‡	‡
5	0.6	6.0	116.0	75.0	‡	‡	‡	‡
Mean	1.1	3.3	70.6	37.6	6.3	8.4	2.4	6.4
25 c.c./Kg./min.								
1	0.5	2.6	3.0	11.9	7.9	8.1	2.2	3.9
30 c.c./Kg./min.								
1	2.3	2.7	6.7	5.2	1.9	2.7	‡	‡
2	0.6	1.4	2.0	4.5	2.2	3.9	1.0	1.6

*E—Epinephrine

†NE—Norepinephrine

‡Blood samples not obtained

§Fibrillation occurred as venae cavae were released. These values not included in means.

In 3 additional experiments in which azygos flow was maintained 15 to 30 minutes, no cardiovascular rebound phenomena were observed. In these animals, contractile force and blood pressure failed to return to control levels.

Several additional azygos flow experiments not included in the above group were performed in which attempts were made to produce ventricular fibrillation during the period of cardiovascular rebound. Digitalization until toxicity in

2 dogs, intravenous procaine hydrochloride in 2 dogs, and generalized hypothermia (28° C.) in 3 dogs were used. In none of 7 dogs did ventricular fibrillation occur.

In 6 experiments using cardiopulmonary bypass at flow rates of 20 to 25 c.c. per kilogram per minute, it was noted that the cardiac rebound occurred in a similar though less intense manner than during azygos experiments (Fig. 2). In 2 bypass experiments at a 30 c.c. flow rate, the contractile force remained at near normal levels during the 10-minute period of bypass. Table I shows that during the experiments with flow rates below 30 c.c. per kilogram per minute, catechol amines were substantially elevated, while relatively little change in amines occurred in the experiments with a flow rate of 30 c.c.

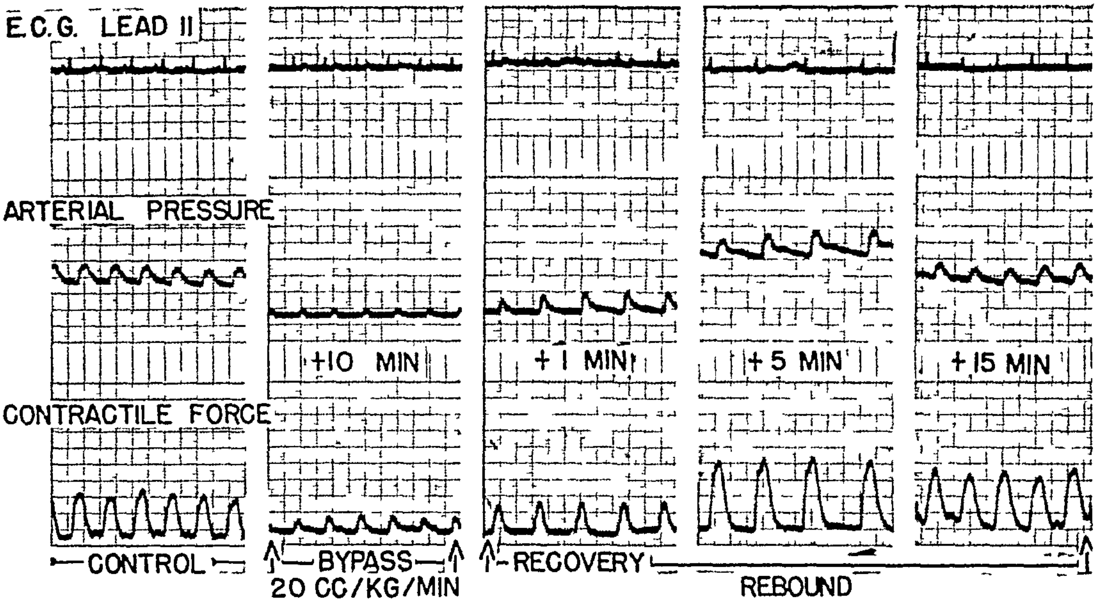

Fig 2.—Effects of bypass on electrocardiogram, myocardial contractile force, and blood pressure See explanation in text

DISCUSSION

Recent investigations concerning cardiac metabolism have altered some of the earlier concepts of the relationship of epinephrine and norepinephrine to the heart. It has been demonstrated that norepinephrine is produced by the postganglionic cardiac sympathetic fibers[8, 15] and also possibly by the chromaffin tissue within the heart itself.[14] The concentration of the amines in the myocardium has been found to consist chiefly of norepinephrine with a lesser amount of epinephrine, the latter averaging approximately 10 per cent[12] As pointed out by Raab,[11] the concentration of these hormones in the myocardium is dependent upon several factors: the intensity of response of the cardiac sympathetic and vagal nerve terminals to stimulation, the absorption of catechol amines from the circulating blood by the heart muscle, the intracardiac formation of these hormones from extraneural sources, and the rate of their enzymatic destruction.

The post ganglionic parasympathetic fibers produce acetylcholine A balance of action of these hormones is maintained within the myocardium Several significant effects of the amines upon myocardial metabolism have been observed (1) norepinephrine causes an increase in myocardial oxygen consumption that is not paralleled by a proportionate increase in cardiac work,[7, 9] and (2) the catechol amines promote anaerobic glycogenolysis that results in the accumulation of lactic acid in the heart muscle[18]

In the experiments reported in this paper the period of decreased blood flow produced relative anoxia throughout the body It is believed that this anoxic condition is the probable stimulus resulting in the rapid discharge of the amines into the general circulation These amines are carried to the heart which is also functioning in a relatively anoxic environment The decreased myocardial perfusion and the anoxia to which the myocardium is subjected results in an increase in anaerobic metabolism and the accumulation of lactic acid and other such metabolites within the heart muscle It has been demonstrated by others[3, 21] that the acidosis produced by low flow rate cardiopulmonary bypass procedures and azygos flow is of the metabolic type Weil and his associates[23] have demonstrated that there is a poor response to sympathomimetic agents in the acidotic patient and dog Thus it may be that the acidosis and the accumulation of lactic acid during conditions of low flow are responsible for the failure of the heart to respond to the increased levels of catechol amines When normal blood flow is restored and coronary perfusion is adequate so that there is correction of the acidosis and the removal of the lactic acid and other metabolites from the myocardium, then the heart is able to respond to the remaining excessive adrenergic amines This same situation has been demonstrated recently in hemorrhagic hypotension[24]

CONCLUSIONS

1 The rebound phenomena have been observed and measured during azygos flow and low flow rate (20 to 25 c c per kilogram per minute) cardiopulmonary bypass procedures

2 The rebound phenomena were found to be associated with an increase in the levels of the plasma epinephrine and norepinephrine

3 The relation between acidosis and the accumulation of lactic acid within the heart during conditions of low flow rate and the response of the heart to the increased levels of catechol amines are discussed

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